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This issue of ZHURNAL OBSHCHEI KHIMII contained an article commemorating the 90th anniversary of the birth of V. I. Lenin. This paper has not been translated inasmuch as it does not contain details of either contemporary Soviet chemical research or its historical development.

PHASE DIAGRAMS OF TERNARY LIQUID SYSTEMS CONTAINING TWO PAIRS OF PARTIALLY MISCIBLE LIQUIDS WITH LOWER CRITICAL SOLUTION TEMPERATURES. III

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Perm' State University
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Original article submitted January 7, 1959

In two previous papers [1, 2], ternary systems were considered which contained two binary systems with lower critical solution temperatures and a third homogeneous boundary system with a normal behavior of the components. We showed theoretically and experimentally that these ternary systems may be characterized by three types of phase diagrams (Types 1a, b, and c) which are shown schematically as isotherms in Fig. 1. In order to illustrate the influence of temperature, the partially miscible regions for each type are shown on a polythermal section through the two-phase regions at a constant composition of component C. The two-phase regions in Fig. 2 are shaded.

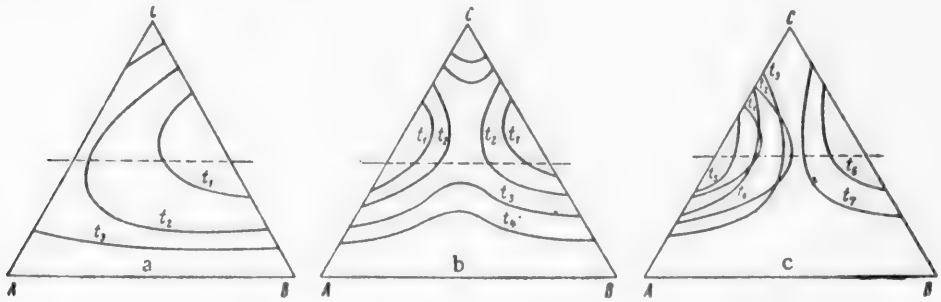

Fig. 1. Possible types of phase diagrams for ternary liquid systems having two binary systems with lower critical solution temperatures and the third binary system with normal behavior of components (Type 1).

The present paper deals with phase diagrams of ternary systems in which chemical reaction occurs between the components of the homogeneous boundary system.

Let us assume that in the ternary system A – B – C (Fig. 3) two of the boundary systems A – C and B – C have miscibility gaps with lower critical solution temperatures, while the third boundary system A – B is homogeneous, with chemical reaction occurring between the components. For the purpose of simplicity we shall also assume that in the liquid phase there is only one chemical compound of composition AB which is not dissociated thermally. In view of this limitation the segments A – AB and AB – B must represent binary systems with normal or close to normal behavior of the components.

A thermally stable compound in the boundary system A – B divides the concentration-composition triangle of the ternary system along the quasi-binary section AB – C into two parts, each of which is an independent ternary system. The components of the quasi-binary system AB – C may behave in different ways toward each

other. They may be completely soluble in each other or they may form a miscibility gap. However, in the ternary systems now being considered, the components of the quasi-binary section usually interact according to the reversible reaction AB + C ⇌ ABC.

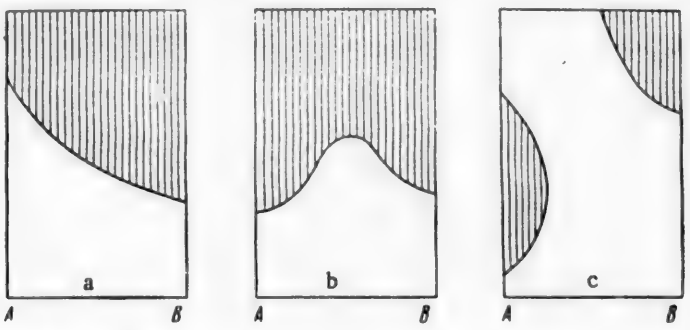

Fig. 2. Polythermal sections of Type 1 phase diagrams (at constant concentration of component C).

The most recent experimental data indicate undoubtedly that ternary systems with chemical interaction of the components of all three boundary systems always have ternary compounds. Like the system A – B, the binary systems A – C and B – C are characterized by chemical interaction of the components, because otherwise it is impossible to explain partial miscibility with a lower critical solution temperature in these systems. Similarly, just as the binary compounds in the partially miscible boundary systems are subject to thermal dissociation, resulting finally in a miscibility gap, so in the quasi-binary section the above mentioned reversible reaction must take place. Lowering the temperature must shift the equilibrium to the right, while a rise shifts it to the left.

Thus, the phase diagrams of these ternary systems will be determined by the physicochemical properties of the components of the quasi-binary section, particularly the thermal stability of the ternary compound and the conditions of mutual solubility.

A. The Quasi-Binary System is Homogeneous

Type 2a. In order for the quasi-binary system AB – C to be completely homogeneous, the components and their reaction product, the ternary compound, must be similar in nature (if only with respect to polarity). Only in this case will any shift in the equilibrium AB + C ⇌ ABC not lead to a miscibility gap in the liquid quasi-binary system. Complete solubility in the quasi-binary system makes possible the existence in the ternary system A – B – C of two separate miscibility gaps which originate at the critical solutions of the boundary systems A – C and B – C. By contrast with Type 1c, the existence of separate miscibility gaps does not depend at all on the relative positions of the critical points of the partially miscible boundary systems. The nodes of the isothermal regions of partial miscibility must lie in the direction of the quasi-binary system because chemical reaction between the components takes place there.

B. Quasi-Binary System with a Lower Critical Solution Temperature

The occurrence of a miscibility gap with a lower critical solution temperature requires, first of all, chemical reaction in the quasi-binary section. This condition is satisfied in the ternary systems being studied. However, there is another necessary condition which requires some similarity in the properties of the binary chemical compound AB and its components, but at the same time a difference with respect to the properties of the third component of the system C such as is observed in the partially miscible boundary systems. Only in this case will the chemical equilibrium AB + C ⇌ ABC result in a homogeneous solution in the quasi-binary system at low temperatures, and at higher temperatures either a miscibility gap with a lower critical point or formation of a closed-ring solubility curve.

The lower critical solution temperature of the quasi-binary system AB – C may vary considerably from those of the partially miscible systems A – C and B – C. Moreover, it is necessary to consider the possible

prevailing influence not only of the homogeneous system A – B, but also of the partially miscible binary systems and the quasi-binary system itself. In short, each of the constituent parts of the ternary system A – B – C may have only one of the previously considered forms of phase diagram inherent in Type 1, and the same directivity of the nodes. It is obvious that combining Type 1 triangles with one another, and analogous triangles with themselves, at the edges with miscibility gaps in the liquid phases, will both, in general, lead to the creation of all the possible varieties of phase diagrams.

Types 2b, c and d. These are formed by combining two Type 1a triangles either along side A – C, along different sides, or, finally, along side B – C. They differ from one another by the relative positions of the lower critical solution temperatures of the quasi-binary system and the partially miscible binary systems.

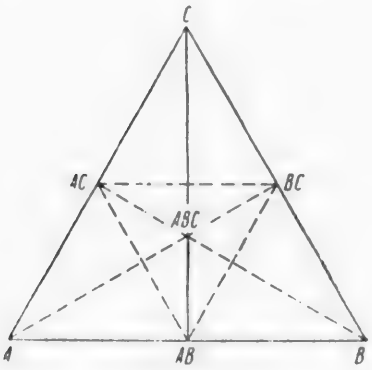

Fig. 3. Geometrical representation of the formation of a ternary compound and of exchange reactions in ternary systems having two binary systems with chemical reaction between the components.

Types 2e, f, and g. These are formed by combining two Type 1b triangles and also by combining a 1b, and a 1a triangle. The first case exemplifies a ternary system in which all three lower critical solution temperatures of the boundary systems and the quasi-binary section are almost the same. In the second case, the temperatures of the critical points of the quasi-binary section and of one boundary system are the same. The other boundary system may have a higher or lower critical solution temperature.

Types 2h - o. These are obtained by combining two 1c triangles with one another or a 1c triangle with 1a and 1b triangles. By combining two 1c triangles there are formed two types (2h and i) of phase diagrams. When 1c and 1a triangles are combined along the sides with miscibility gaps, four variants (2j, k, l, and m) are theoretically possible. Finally, by combining 1c and 1b triangles two types (2n and o) are obtained.

For the purpose of summarizing the graphical material, we did not consider it necessary to present the isotherms because on the basis of what has been said above they are self-evident. Nevertheless, for an appreciation of the form of the surface which separates the two-phase region from that of homogeneous solutions, we have represented each arrangement of the system by a polythermal section, just as was done for Type 1. In Fig. 4, such a polythermal section is given for type 2a, and in Fig. 5 for all the remaining ones. The letters designating the polythermal sections correspond to those designating the type. In all cases, the shaded areas indicate the two-phase regions. We shall use this method of representing the phase diagrams again later.

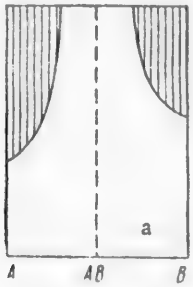

Fig. 4. Polythermal section of Type 2 ternary systems (at constant concentration of component C), when the quasi-binary system is homogeneous.

In conclusion, it should be noted that individual types of phase diagrams will take precedence over others. One will be encountered very frequently and others less often, but this does not mean that some of them may not actually exist. All diagrams, because they are formed by a rational system A – B, must have singular points in the partially miscible region in the quasi-binary section. Such geometrical diagrams will be obtained when there is a thermally dissociated compound in the homogeneous system A – B. In this case, however, the elements of singularity will be absent in the phase diagrams. Poor stability in the compound AB, which is quantitatively indicated by a considerable displacement of the exchange reactions $AB + C \rightleftharpoons AC + B$ and $AB + C \rightleftharpoons BC + A$ to the right, will lead to a decrease in the number of the above-mentioned phase diagrams of Type 1 ternary systems.

C. Quasi-Binary System with Upper Critical Solution Temperature

Let us assume that the quasi-binary system AB – C has a miscibility gap in liquid phases with an upper critical solution temperature. The closing of the binodal curves toward a lower critical temperature proceeds

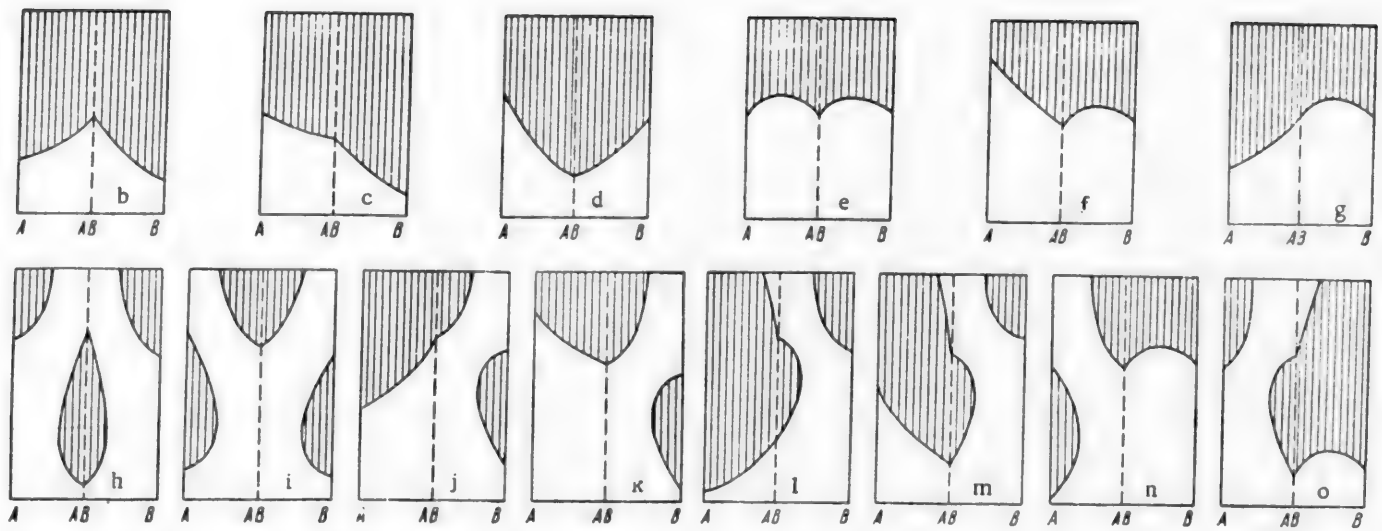

Fig. 5. Polythermal sections of Type 2 ternary systems (at constant concentration of component C), when the quasi-binary system has a miscibility gap with a lower critical solution temperature.

infinitely gradually, and consequently is not attained in practice. Such an assumption is apparently well founded because binary systems are known which are characterized by chemical reaction of the components, and at the same time by a miscibility gap having an upper critical solution temperature.

This makes it possible to consider the ternary systems being studied as consisting of two parts each of which is formed from two partially miscible boundary systems with differently directed critical points. Such ternary systems were studied in detail in one of our communications [3]. It was shown that when the components of the boundary homogeneous system behave normally, there must be four variants of the phase diagram depending upon the relative positions of the critical points of the partially miscible binary systems and upon the directivity of the exchange reaction.

Let us assume that in the system A−B−C (Fig. 6) the binary system A−B is homogeneous with normal behavior of the components. The other two boundary systems have partially miscible regions, the system A−C having a miscibility gap with a lower critical solution temperature and the system B−C an upper. In addition, let us assume that in the system B−C the components react chemically. Under such conditions, in the ternary system A−B−C, the exchange reaction AC + B ⇌ BC + A must take place.

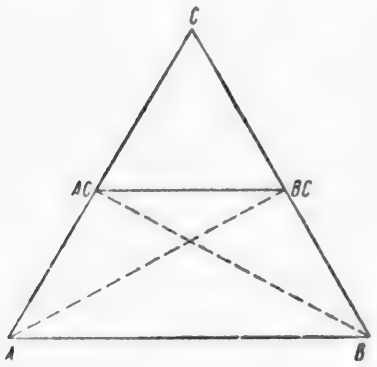

Fig. 6. Geometrical representation of the exchange reaction in ternary systems in which the components of two boundary systems react chemically.

When this reaction is shifted considerably to the right, two types of phase diagrams must be expected. The difference between them is determined only by the positions of the critical solution temperatures of the partially miscible boundary systems. Both types are shown in Fig. 7a and b in the form of projections of individual isotherms and of one polythermal section (at constant composition of component C), for each type of system. If the exchange reaction is shifted in the reverse direction, then, in addition to the type illustrated in Fig. 7a, two new types appear as shown in Fig. 7c and d.

It is now understandable how the ternary systems which we are studying, and which have a miscibility gap in the quasi-binary section, with an upper critical solution temperature, can be formed by combining types described above. However, the directivity of the exchange reaction must not be overlooked when the possible types of phase diagrams are being derived for such systems. Actually, in the system A−B−C (see Fig. 3) having one boundary system A−B with a thermally undissociated compound AB and two partially miscible boundary systems A−C and B−C with lower critical solution temperatures, and consequently with chemical interaction of the components, there must exist at least one ternary compound. The quasi-binary system AB−C is a stable median and divides the composition triangle of the system into two secondary systems in each of which an exchange reaction occurs. In the triangle A−C−AB the exchange reaction ABC + A ⇌ AB + + AC is geometrically represented by the quadrilateral A−AC−ABC−AB; in the triangle AB−C−B the exchange reaction ABC + B ⇌ AB + BC is geometrically represented by the quadrilateral AB−ABC−BC−B. Both reactions are reversible and depending upon the nature of the substances and equilibrium conditions there is the possibility of both being shifted simultaneously to the right or to the left, or one may be shifted to the right and the other to the left.

Types 2p - r. If both reactions are reversed, then the whole ternary system is formed by combining two Type 1 triangles of the forms 7a and 7b with themselves, or with each other, along the B−C sides. It is obvious that there can be only three combinations and therefore only three types of phase diagrams.

Types 2s - v. If one exchange reaction is shifted to the right and the other to the left, then the whole ternary system must be formed by combining along the B−C sides each of the 7b, 7c, and 7d triangles with one of the 7a or 7b forms. Six arrangements of phase diagrams are thus possible. Two of these are identical with types 2p and 2r. The four others are indicated above.

Types 2w - y. If both exchange reactions are shifted to the right, the phase diagrams of the whole system are formed by combining 7b, 7c, and 7d triangles with themselves and with one another. Six combinations are thus possible, three of which are identical with types 2p, 2s, and 2t. Three new ones are indicated above.

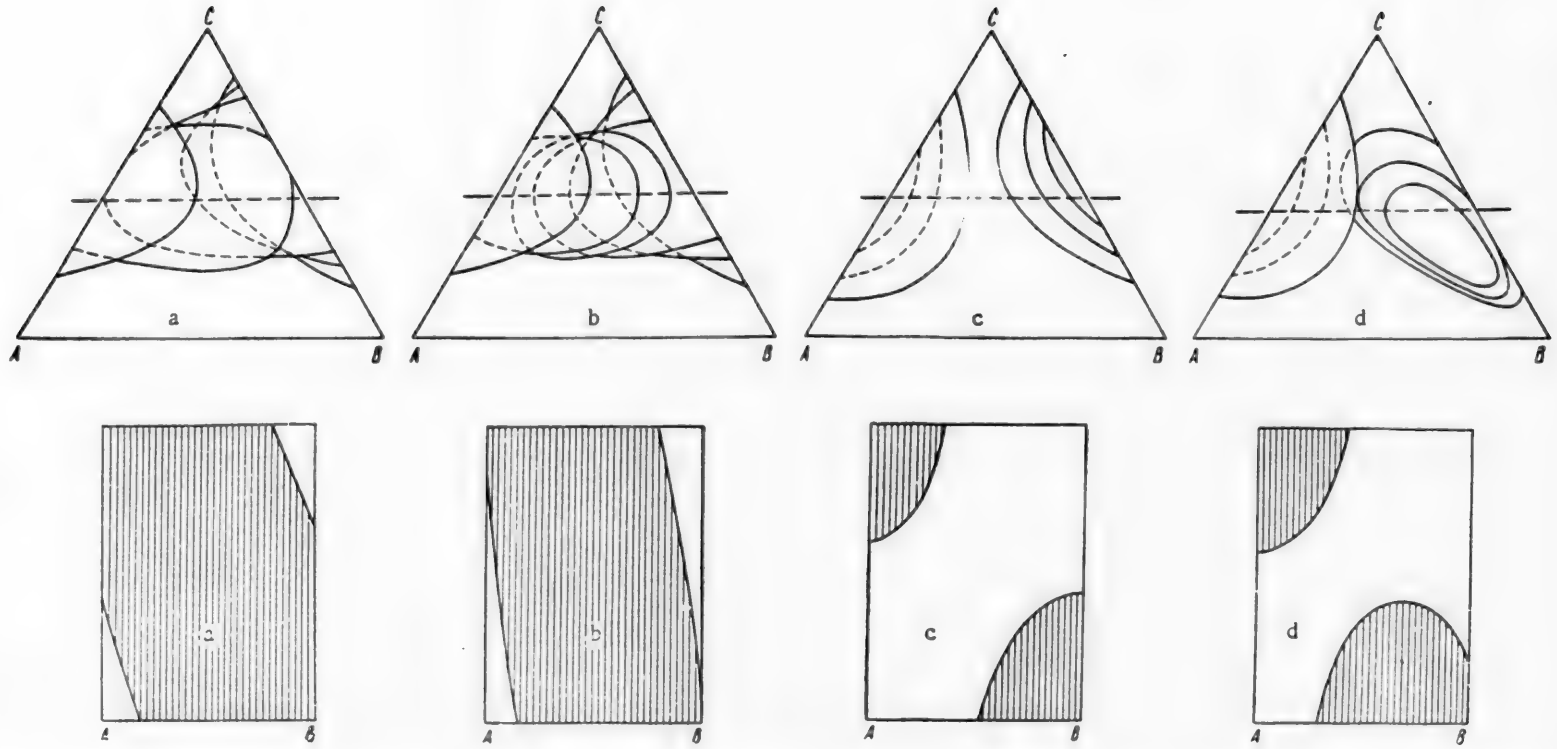

Fig. 7. Isothermal and polythermal sections of phase diagrams of ternary systems composed of two partially miscible binary systems with differently directed critical points and a third homogeneous system with normal behavior of the components.

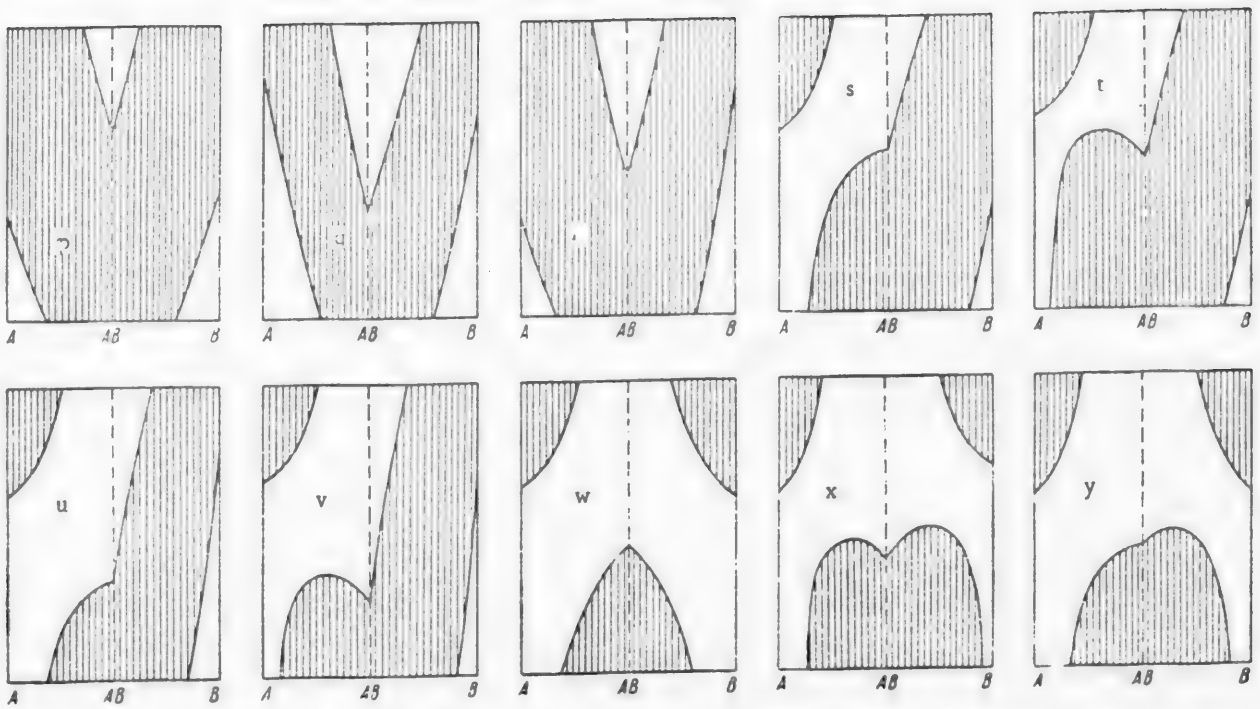

Fig. 8. Polythermal sections of Type 2 ternary systems (at constant concentration of component C), when the quasi-binary system has a miscibility gap with an upper critical solution temperature.

Since the above descriptions permit the isotherms of the ternary systems studied to be visualized without much difficulty, such graphical material as was done previously has been omitted from the present paper. We consider it sufficient for the purpose of understanding the spacial arrangements of the partially miscible regions to show one polythermal section for each type. These are given in Fig. 8 in which the letters correspond to the type designation.

We have noted that four types (2p, 2r, 2s, and 2t) are analogous to five others. This similarity appears only in the polythermal sections of the partially miscible regions. In fact, their phase diagrams are somewhat different. This difference is due to the presence or absence of retrogradation in the isothermal lines of the partially miscible regions, in the whole system, as well as the constituent parts.

It should be pointed out that these phase diagrams for ternary liquid systems will be obtained also in the case of a dissociating compound AB. However, in such systems the elements of singularity in the partially miscible regions will probably be absent. A marked decrease in chemical reactivity of the components of the homogeneous system A – B, quantitatively shown by shifting of the equilibrium of the reaction $AB + 2C \rightleftharpoons AC + BC$ to the right, will lead to a decrease in the number of types of phase diagrams in Type 1 ternary systems.

SUMMARY

Possible types of phase diagrams have been considered for ternary liquid systems composed of two partially miscible binary systems with lower critical solution temperatures and a third homogeneous binary system with chemical interaction of the components.

LITERATURE CITED

1. E. F. Zhuravlev, Zhur. Obshch. Khim. 30, 12 (1960).*
2. E. F. Zhuravlev, Zhur. Obshch. Khim. 30, 7 (1960).*
3. E. F. Zhuravlev, Khimiya i Khim. Tekh. (in press).

*See C. B. translation.

THE CRYOSCOPIC METHOD OF DETERMINING MOLECULAR WEIGHTS

THE BINARY SYSTEM ANILINE – ACETIC ACID

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1070-1075, April, 1960
Original article submitted September 15, 1958

Physicochemical studies of the binary system aniline–acetic acid depict it as one in which the components react chemically. The fusion curve of this system, which was investigated by O'Connor [1], has two maxima. One of these corresponds to a solid melting at 16.7° and having the composition $C_6H_5NH_2 \cdot 2C_2H_4O_2$, while the second maximum lies in a metastable region and corresponds to the composition $2C_6H_5NH_2 \cdot C_2H_4O_2$ and melting point − 19.4°.

Chemical interaction of aniline and acetic acid is also indicated in the isotherms of different physical properties of this system. Thus, D. P. Konovalov [2] found that the heat of mixing and the heat capacity isotherms have maxima at 38 mole % of aniline, and that the electrical conductivity isotherm is characterized by two breaks and one maximum. D. P. Konovalov showed that the breaks and the maximum on the electrical conductivity isotherms correspond to simple molecular proportions: $C_6H_5NH_2 \cdot 6C_2H_4O_2$, $C_6H_5NH_2 \cdot 3C_2H_4O_2$, $2C_6H_5NH_2 \cdot 3C_2H_4O_2$. These results were confirmed by N. A. Trifonov and S. I. Cherbov [3].

The viscosity of this system was investigated by Faust [4]. The viscosity isotherms have a sloping maximum which shifts with temperature at about 30 mole % of amine. V. Ya. Anosov [5] studied this system by means of the refractive index and showed that the maximum deviation from additivity occurs at 62 mole % of aniline.

E. F. Zhuravlev [6] investigated the solubility of the above system in benzene. It was found that the chemical compound $2C_6H_5NH_2 \cdot C_2H_4O_2$ is indicated by a synclinal fold in the partially miscible region of this ternary system. Two maxima in solubility of the liquid phases, leading at higher temperatures to formation of two independent miscibility gaps with upper ternary critical points, correspond to complexes of the binary system: $C_6H_5NH_2 \cdot 3C_2H_4O_2$ and $6C_6H_5NH_2 \cdot C_2H_4O_2$.

Undoubtedly, the facts presented above indicate chemical reaction between aniline and acetic acid, and also that this binary system is characterized by a very complex physicochemical behavior of the components: depending upon the concentrations of the substances and the temperature conditions, there may exist a rather large number of products of mutual association. However, different methods of physicochemical investigation reveal only some details of the general picture of the chemical interactions. This must explain the apparent contradictions which arise during experimental studies of the various properties of the present system.

For the purpose of supplementing the physicochemical data on the aniline – acetic acid system, we decided to study it by determining the molecular weight cryoscopically, using solvents with different melting points. Benzene and naphthalene were selected for this purpose.

The determination of molecular weight, as a method of physicochemical analysis, was used successfully by V. V. Udovenko [7] and his students. By constructing molecular weight composition diagrams of the binary system, these authors, in a large number of admittedly selected systems, showed graphically the existence of a relationship between the molecular weight curves at fixed concentrations and the nature of the mutual behavior of the substances. In all the molecular weight studies on binary systems the above-mentioned authors used the

same solvent – benzene. E. F. Zhuravlev and M. N. Bychkova [8] showed that the choice of solvent is very important: results obtained using various solvents may differ not only quantitatively but also qualitatively. In view of this fact, we selected two solvents with quite different melting points for determining molecular weights in the aniline – acetic acid system. In this way we hoped to learn how the stability of individual mutual association products in this system varies with the temperature as well as the nature of the solvent.

EXPERIMENTAL

Acetic acid was prepared by reacting equimolar quantities of freshly distilled acetic anhydride and water; the mixture was boiled in a flask under reflux for 8 hours, after which the acetic acid was distilled. The product had a constant boiling point of 118.0° and a melting point of 16.6°. The aniline after drying was distilled, and the fraction boiling at 182.5° (748 mm) was used in the experiments. The benzene was of cryoscopic purity and the naphthalene was twice sublimed. The cryoscopic measurements were made with a Beckmann apparatus. Benzene solutions were cooled with a salt-ice mixture, and with naphthalene boiling water served as a thermostatic fluid. Molecular weights were calculated as described in [9]. The concentration of the solute was expressed as moles per 1000 g of solvent.

Results of the experimental investigation are given in Tables 1 and 2. They are represented graphically in Figs. 1 and 2. The molarity of the solute is shown on

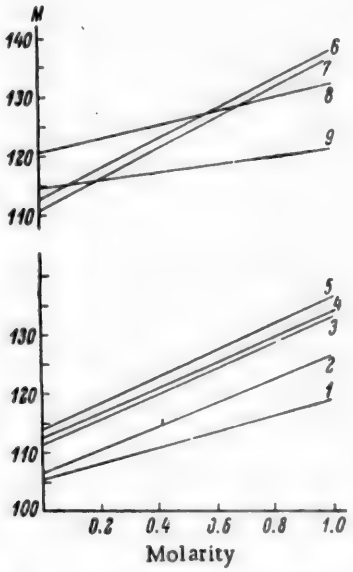

Fig. 1. Dependence of molecular weight of the binary system aniline – acetic acid on concentration in benzene solution.

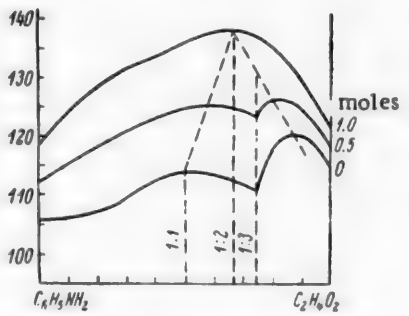

Fig. 2. Molecular weights of the binary system aniline – acetic acid at fixed concentrations in benzene.

one axis and molecular weight on the other axis. Figures 2 and 4 show the system aniline – acetic acid as isomolar sections of the ternary systems.

Determination of the Molecular Weight of Aniline and Acetic Acid in Benzene and Naphthalene

In Table 1 data are presented on the determination of the molecular weight of aniline and acetic acid dissolved in benzene. In Fig. 1, the dependence of the molecular weight upon concentration of solution is presented in graphical form (Curves 1 and 9, respectively). Analogous data for naphthalene solutions are presented in Fig. 3 (Curves 1 and 7).

The results of this investigation show that the molecular weight of aniline in benzene solution as found by the cryoscopic method is much higher than its molecular weight calculated from its formula; it increases markedly with the concentration of aniline in the solution, but even at infinite dilution it remains 10-12 units higher than the formula weight. The molecular weight of aniline changes comparatively slightly with increase in concentration of the naphthalene solution, and at infinite dilution it is equal to the theoretical value.

The experimental value of the molecular weight of acetic acid is much higher than the formula weight. At infinite dilution of acetic acid with benzene and naphthalene its molecular weight approaches the value of 115 units. This almost corresponds to the formula $(C_2H_4O_2)_2$. Our observations are in complete agreement with the results of numerous other studies of the association of acetic acid in the vapor and liquid states as well as in aqueous solutions [10-14]. We have found that the molecular weight of acetic acid exceeds 120 units at concentrations greater than 0.8 M in benzene and 0.4 M in naphthalene. This shows that association of the acetic acid molecule in the liquid phase is not limited to the formation of dimers.

TABLE 1

Molecular Weight of the System Aniline–Acetic Acid in Benzene Solutions

No. of curve in Fig. 1	Content acetic acid in binary system (mole%)	No. moles substance in 1000 g benzene	Δt	M
1	0.0	0.20	0.896	108.3
		0.41	1.726	110.5
		0.59	2.395	113.6
		0.74	2.902	115.3
		0.97	3.668	118.3
2	14.8	0.27	1.049	113.5
		0.52	1.915	117.0
		0.72	2.562	120.5
		0.94	3.214	123.6
3	33.3	0.31	1.080	118.4
		0.45	1.565	121.3
		0.55	1.810	123.2
		1.02	3.050	132.3
4	40.0	0.18	0.635	116.3
		0.53	1.688	123.6
		0.80	2.425	129.4
		1.01	2.920	133.9
		1.19	3.315	138.8
5	50.2	0.19	0.610	118.3
		0.38	1.180	122.3
		0.72	2.100	129.3
		0.96	3.348	135.2
6	66.5	0.27	0.800	118.8
		0.52	1.465	125.7
		0.78	2.072	131.7
		1.02	2.560	138.7
7	75.0	0.19	0.545	116.4
		0.32	0.920	119.3
		0.48	1.305	123.2
		0.81	2.065	132.1
		1.05	2.525	138.6
8	85.0	0.16	0.428	120.7
		0.52	1.310	126.9
		0.84	2.080	130.7
		1.16	2.693	135.9
		1.42	3.163	139.9
9	100.0	0.17	0.438	115.7
		0.49	1.233	118.2
		0.72	1.778	119.2
		1.04	2.501	121.8
		1.45	3.383	124.0

TABLE 2

Molecular Weight of the System Aniline–Acetic Acid in Molten Naphthalene

No. of curve in Fig. 3	Content acetic acid in binary system (mole%)	No. moles substance in 1000 g of naphthalene	Δt	M
1	0.0	0.14	0.940	93.7
		0.41	2.685	94.0
		0.51	3.568	94.6
		0.70	4.385	94.8
2	15.0	0.30	1.882	92.9
		0.43	2.668	93.6
		0.57	3.365	96.0
		0.71	4.092	97.5
3	33.4	0.35	1.958	97.2
		0.55	2.948	99.7
		0.69	3.572	101.2
		0.80	4.210	101.6
4	50.0	0.19	1.073	94.3
		0.34	1.808	96.8
		0.49	2.490	100.0
		0.64	3.118	102.6
		0.95	4.306	107.4
5	66.6	0.25	1.240	97.4
		0.44	2.020	101.6
		0.63	2.730	107.5
		0.85	3.390	113.2
6	85.0	0.17	0.729	104.7
		0.32	1.295	107.4
		0.51	1.950	110.9
		0.85	3.025	118.4
7	100.0	0.20	0.700	116.7
		0.45	1.550	120.0
		0.74	2.357	123.4
		1.06	3.232	127.3
		1.45	4.170	132.9

Determination of the Molecular Weight of the Binary System

Benzene Solutions. The relationship between molecular weight and molarity of the solution is linear over the range of concentrations studied (Fig. 1). The molecular weights of complexes in the binary system are higher than the molecular weight of the pure substances. This is a definite indication of chemical reaction between the amine and acetic acid.

Chemical reaction between aniline and acetic acid is more strikingly revealed by plotting sections of the ternary system at fixed concentrations. Such a section at infinite dilution is shown in Fig. 2 and it is characterized by two maxima and one minimum. These molecular weight maxima correspond to the compounds $C_6H_5NH_2 \cdot C_2H_4O_2$ and $C_6H_5NH_2 \cdot 6C_2H_4O_2$, and the minimum corresponds to the compound $C_6H_5NH_2 \cdot 3C_2H_4O_2$. These compounds are, therefore, the most stable ones in dilute solutions. As the concentration of the binary system aniline – acetic acid, increases, the maxima and the minimum gradually disappear, the minimum remaining at the same composition and the two maxima approaching each other. At concentrations above 0.7 M they blend into one maximum corresponding to the formula $C_6H_5NH_2 \cdot 2C_2H_4O_2$. This compound is the most stable in the liquid phase at low temperatures and high concentrations of the binary system aniline – acetic acid. As we have noted above, it also appears on the fusion curve in the form of a maximum.

Our experimental data show that the system aniline – acetic acid is related to typical irrational systems having a series of association products. All the compounds found have molecular weights below the theoretical values. Even at low temperatures the reactions between amine and acid in the liquid phase are reversible. However, it must be kept in mind that these compounds are subject not only to thermal but probably also to electrolytic dissociation: it is impossible, otherwise, to explain the minimum on the molecular weight curves. The compound $C_6H_5NH_2 \cdot 3C_2H_4O_2$ is the most polar. Benzene causes it to dissociate electrolytically and the more it is diluted by the solvent, the smaller is its observed molecular weight. Our conclusions are in complete agreement with investigations of this system by electrical conductivity and its solubility in slightly polar solvents: electrical conductivity isotherms have maxima corresponding to the compound $C_6H_5NH_2 \cdot 3C_2H_4O_2$. The maximum in the liquid phase solubility gap of the system aniline – acetic acid – benzine corresponds to this same compound [6].

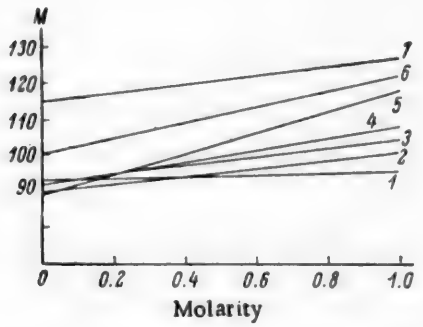

Fig. 3. Dependence of molecular weight of the binary system aniline – acetic acid on concentration in molten naphthalene.

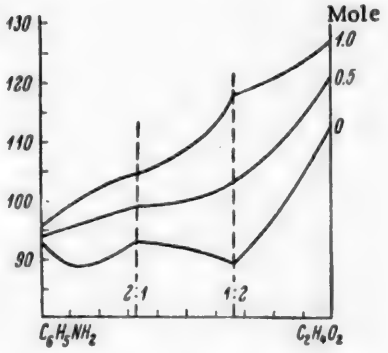

Fig. 4. Molecular weights of the binary system aniline – acetic acid at fixed concentrations in molten naphthalene.

Solutions in Molten Naphthalene. The relationship between molecular weight and molarity of the solution is linear over the range of concentrations studied (Fig. 3). The molecular weight of isomolar mixtures increases from the amine to the acetic acid. However, at low concentrations, several lines intersect one another. Hence, the molecular weights of complexes in the binary system aniline – acetic acid vary with the concentrations of amine and acid and are not completely additive. This is eloquently illustrated by the molecular weight curves in Fig. 4.

The molecular weight curves of this system are characterized by discontinuities which correspond exactly to the compounds $2C_6H_5NH_2 \cdot C_2H_4O_2$ and $C_6H_5NH_2 \cdot 2C_2H_4O_2$. Evidently, these are the most stable compounds of amine and acid in the liquid phase at high temperatures. These are the same compounds which appear in fusion studies of this system. The apparent molecular weights of the compounds are very low. The values given by the molecular weight curves at infinite dilution are less than the molecular weights of the pure components of the system. This phenomenon is probably caused not only by decomposition of the amine – acid compounds into the original substances due to the action of the elevated temperature and the solvent, but also possibly by electrolytic dissociation.

It is very interesting to note that the angles of intersection of the molecular weight curves which correspond to compound formation change direction with a change in concentration of the solutions. At low concentrations of the compound $C_6H_5NH_2 \cdot 2C_2H_4O_2$ the angle of intersection of the molecular weight curves is turned toward the composition axis of the system, and at high concentrations in the opposite direction. On the other hand, at low concentrations of the compound $2C_6H_5NH_2 \cdot C_2H_4O_2$, the intersection angle is turned away from the composition axis, and at high concentrations toward the composition axis. This is explained by a change in the stability constants of the compounds in the solutions. The molecular weight of the second compound increases comparatively slowly with increasing concentration, but much faster in the case of the first compound. Thus, this compound is the more stable at high temperatures in its own liquid phase.

SUMMARY

1. The binary system aniline – acetic acid in benzene and naphthalene has been studied by molecular weight measurements.

2. The experimental data indicated that this is an irrational system in which the components associate to form a series of compounds. Chemical compounds of the following compositions appeared distinctly on the molecular weight curves: $2C_6H_5NH_2 \cdot C_2H_4O_2$, $C_6H_5NH_2 \cdot C_2H_4O_2$, $C_6H_5NH_2 \cdot 2C_2H_4O_2$, $C_6H_5NH_2 \cdot 3C_2H_4O_2$ and $C_6H_5NH_2 \cdot 6C_2H_4O_2$.

3. It was shown that the presence of chemical compounds is indicated not only by maxima but also by minima on the molecular weight curves. Minima appear when the compounds seem to be electrolytes.

LITERATURE CITED

1. E. A. O'Connor, J. Chem. Soc. 119, 400 (1921).
2. D. P. Konovalov, Zhur. Russ. Khim. Obshchestva 24, 440 (1892); 25, 212 (1893).
3. N. A. Trifonov and S. I. Cherbov, Izvest. Perm. Biol. Inst. 6, 5 (1928).
4. Faust, Z. Phys. Chem. 79, 97 (1912).
5. V. Ya. Anosov, Uch. Zap. Sarat. GU 6, 3 (1927).
6. E. F. Zhuravlev, Zhur. Fiz. Khim. 12, 639 (1938).
7. V. V. Udovenko, Zhur. Obshch. Khim. 18, 586 (1948); 18, 572 (1948).
8. E. F. Zhuravlev and M. N. Bychkova, Uch. Zap. Perm. GU 8, 17 (1954).
9. V. V. Udovenko, Zhur. Obshch. Khim. 11, 276 (1941).
10. M. S. Vrevskii, K. P. Mishchenko, and B. A. Muromtsev, Zhur. Russ. Khim. Obshchestva 59, 598 (1927).
11. M. I. Batuev, Izvest. Akad. Nauk SSSR, Ser. Fiz. 12, 611 (1948); Doklady Akad. Nauk SSSR 59, 1117 (1948).
12. S. Feneant, Compt. rend. 235, 1292 (1952).
13. A. A. Glagoleva and A. A. Ferkhman, Zhur. Obshch. Khim. 28, 289 (1958).*
14. D. R. Cartwright and C. B. Monk, J. Chem. Soc. (1955), p. 2500.

* Original Russian pagination. See C. B. translation.

INVESTIGATION OF ORGANIC-ACID SALTS

II. THE TERNARY SYSTEM

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Original article submitted January 29, 1959

Low-melting salt mixtures are of interest for a number of practical purposes and are convenient subjects for physicochemical investigations. Sodium and potassium acetates withstand heating to 350° and, briefly, even to 400°. Cadmium halides differ in their ability to form autocomplexes. In character they are transitional from typical heteropolar salts to nonelectrolyte salts.

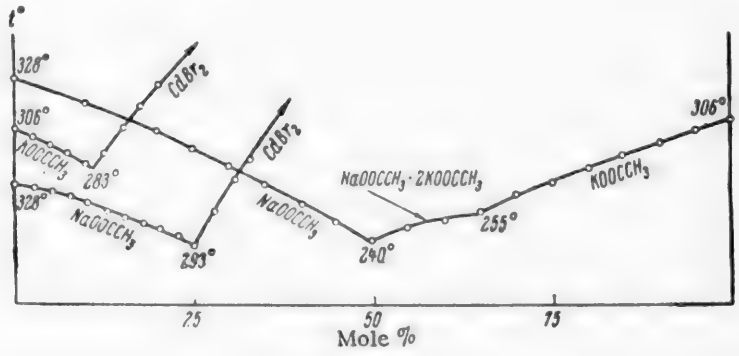

Fig. 1. Collateral binary systems.

The investigated system sodium acetate – potassium acetate – cadmium bromide has the character of a ternary system, but besides, it is a stable diagonal cross section of the triangular prism of composition of the quaternary reciprocal system Na, K, Cd ‖ Br, CH_3COO.

EXPERIMENTAL

The method of investigation was described earlier [1]. Melting points of the salts: $NaOOCCH_3$ 328°, $KOOCCH_3$ 306°, and $CdBr_2$ 568°. For brevity, only part of the experimental data are given in the tables. All composition data are given in equivalent percentages.

Binary Systems

1. $NaOOCCH_3$ – $KOOCCH_3$ (see the preceding article [1]). Contrary to earlier data [2, 3], the system forms the incongruently melting compound $NaOOCCH_3 \cdot 2KOOCCH_3$. The eutectic point corresponds to 240° and 50% $KOOCCH_3$. The transition point is 255° and 65% $KOOCCH_3$ (Fig. 1).

Internal Sections and Binary Systems

Section I		Section II		Section III		Section IV		Section V		Sides			
50% $(KOOCCH_3)_2$ 50% $(NaOOCCH_3)_2$		25% $(NaOOCCH_3)_2$ 75% $(KOOCCH_3)_2$		42.5% $(NaOOCCH_3)_2$ 57.5% $(KOOCCH_3)_2$		32.5% $(KOOCCH_3)_2$ 67.5% $(NaOOCCH_3)_2$		15% $(KOOCCH_3)_2$ 85% $(NaOOCCH_3)_2$		$(KOOCCH_3)_2$–$CdBr_2$		$(NaOOCCH_3)_2$–$CdBr_2$	
% $CdBr_2$	t	% $CdBr_2$	t	% $CdBr_2$	t	% $CdBr_2$	t	% $CdBr_2$	t	% $CdBr_2$	t	% $CdBr_2$	t
0.0	240°	0.0	271°	0.0	248°	0.0	276°	0.0	306°	0.0	306°	0.0	328°
2.5	235	2.0	265	2.0	243	2.5	275	5.0	302	2.5	300	5.0	323
5.0	250	4.0	259	4.0	236	5.0	274	10.0	299	5.0	296	10.0	317
7.5	282	5.0	256	5.0	247	7.5	282	15.0	292	7.5	292	15.0	310
10.0	300	7.5	273	7.5	280	12.5	308	17.5	296	10.0	285	20.0	303
12.5	313	12.5	308	10.0	300	17.5	330	22.5	318	12.5	291	25.0	293
15.0	328	15.0	320	12.5	319	20.0	342	27.5	344	15.0	306	27.5	312
										20.0	329	32.5	342

Note: t is the temperature of appearance of the first crystals.

2. $(NaOOCCH_3)_2 - CdBr_2$ was studied by us; it is a quasi-binary system, being a stable diagonal of the reciprocal system Na, Cd || Br, CH_3COO. The eutectic corresponds to 293° and 75% $(NaOOCCH_3)_2$ (Fig. 1, table).

3. $(KOOCCH_3)_2 - CdBr_2$ was studied by us. It is a stable diagonal of the reciprocal system K, Cd || Br, CH_3COO. The eutectic corresponds to 283° and 88.5% $(KOOCCH_3)_2$ (Fig. 1, table).

Ternary System

$(NaOOCCH_3)_2 - (KOOCCH_3)_2 - CdBr_2$. Five internal sections were investigated (Fig. 2, table), and on the basis of these the phase diagram of the ternary system was constructed. The crystallization surface consists of four fields having in common a triple eutectic point at 229° and 4% $CdBr_2$, 48% $(NaOOCCH_3)_2$, and 48% $(KOOCCH_3)_2$ and a transition point at 242° and 4.5% $CdBr_2$, 33% $NaOOCCH_3$, and 62.5% $(KOOCCH_3)_2$.

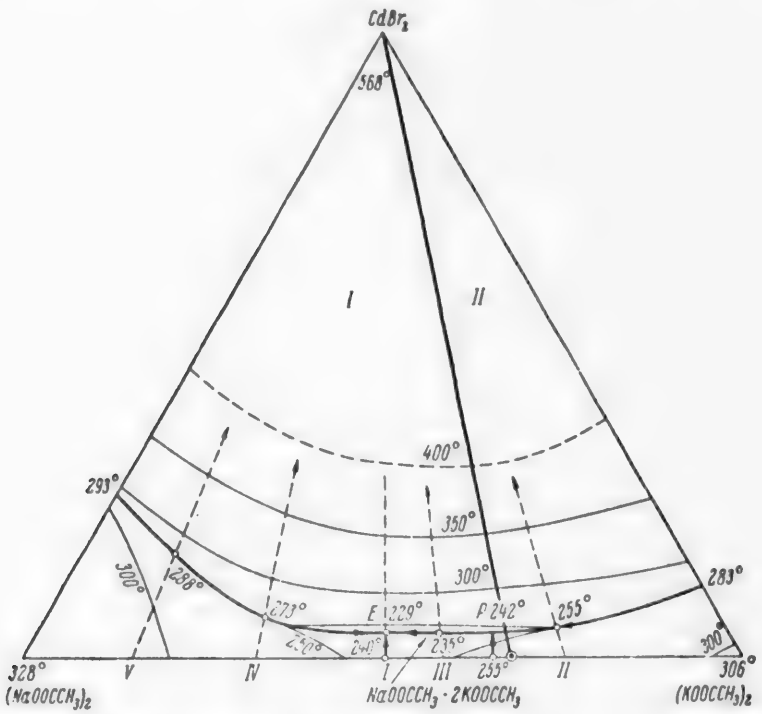

Fig. 2. Phase diagram of the ternary system $(NaOOCCH_3)_2 - (KOOCCH_3)_2 - CdBr_2$; disposition of internal sections and triangulation.

The system is divided by the triangulating section $CdBr_2 - NaOOCCH_3 \cdot 2KOOCCH_3$ into two triangles with a common side: I) $NaOOCCH_3 - CdBr_2 - NaOOCCH_3 \cdot 2KOOCCH_3$ and II) $NaOOCCH_3 \cdot 2KOOCCH_3 - CdBr_2 - KOOCCH_3$.

The isotherms within the fields of the components bulge away from the composition apex. In its general character the diagram of this ternary cross section is a stable, diagonal cross section of the quaternary reciprocal system Na, K, Cd || Br, CH_3COO. Melts of this system are stable up to 350° and may be heated briefly to 400°, but in this case appreciable decomposition occurs, minute gas bubbles being evolved.

SUMMARY

The system sodium acetate – potassium acetate – cadmium bromide was studied. In the phase diagram of the system there are four crystallization fields having in common a triple eutectic point at 229° and a transition point at 242°.

LITERATURE CITED

1. I. I. Il'yasov and A. G. Bergman, Zhur. Obshch. Khim. 30, 355 (1960).*
2. A. V. Baskov, Zhur. Russ. Fiz.-Khim. Obshchestva 47, 1953 (1915).
3. G. G. Diogenov, Zhur. Neorg. Khim. 1, 799, 2551 (1956).

* Original Russian pagination. See C. B. translation.

INVESTIGATION OF PHASE EQUILIBRIA IN THE SYSTEM ANTHRANILIC ACID – WATER – ETHANOL

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The simplest form of metastable equilibria between liquid phases was found in the ternary system salicylic acid – water – ethanol [1]. In the diagram of state of the system the volume, corresponding to metastable equilibria, begins at the plane of the binary system (salicylic acid – water) and ends within the prism of the ternary system; it has no special geometric elements. Anthranilic acid is similar to salicylic acid in its molecular structure and its behavior in binary systems with water (see below). On the strength of this it might be supposed that their ternary systems with aqueous-alcoholic solvents would present similar pictures of phase equilibria. To elucidate the given question, the ternary system anthranilic acid – water – ethanol was investigated with regard to stratification and melting point in the present work.

EXPERIMENTAL

Of the binary systems which are components of the given ternary one, the system water – ethanol was described in detail earlier [1]. It belongs to the class of systems with simultaneous decomposition of associated components and chemical interaction. The system anthranilic acid – water was investigated with regard to melting point and stratification [2]. In it (as in the system with salicylic acid) a curve of metastable liquid-phase equilibrium, with an upper critical point at 78° and an anthranilic acid content of 38%, was found. The system anthranilic acid – ethanol was studied with regard to melting point in the present work.

TABLE 1
Equilibrium in the System Anthranilic Acid – Ethanol

Anthranilic acid (wt. %)	Crystallization temperature
40.11	60.5°
49.87	73.0
59.91	85.0
70.00	97.5
80.11	111.0
90.00	124.5
100.00	145.0

The following reagents were used: anthranilic acid, m. p. 145°, redistilled water, and distilled 96% ethanol, b. p. 78°; the latter was not dehydrated, since aqueous-alcoholic mixtures were prepared from it, the water contained in it being taken into account.

Investigations with regard to stratification were carried out by V. F. Alekseev's visual-polythermal method [3] in sealed glass ampules in a glycerol thermostat, crystallization being delayed. The latter was studied in the same ampules.

In the System Ethanol – Anthranilic Acid, crystallization of the latter was studied in the interval from its melting point to 60° by the Shreder method [4], and also by the method of internal priming [5]. Numerical data obtained are given in Table 1; the crystallization curve is shown in Fig. 1 (Curve 0). The latter drops sharply downward; this indicates that the solubility of salicylic acid in ethanol depends only slightly on temperature.

The Ternary System Anthranilic Acid – Water – Ethanol was studied with regard to stratification and melting point (by the indicated methods) through the investigation of polythermal sections through its prism,

passing from the anthranilic acid edge to the face of the binary system water – ethanol. Numerical data obtained are given in Table 2; the polytherms are shown in Fig. 1, in which melting-point (Cr) and stratification (St) curves of the system anthranilic acid – water are given. Stratification was found only in the case of the first two sections. The stratification polytherms are qualitatively similar to the stratification curve of the system anthranilic acid – water. On moving from the latter to the second section they bound all smaller regions of liquid-phase equilibria and have decreased upper consolute temperatures. The crystallization curves of the ternary mixtures drop sharply downward, but in sections with stratification over the crystallization curves, the latter have gently sloping portions.

TABLE 2

Polytherms of the Ternary System Anthranilic Acid – Ethanol – Water

Anthranilic acid (wt. %)	Temperature		Anthranilic acid (wt. %)	Temperature	
	of stratification	of crystallization		of stratification	of crystallization
Section 1: 10% ethanol, 90% water			Section 3: 40% ethanol, 60% water		
10.21	—	85.0°			
20.04	65.0°	87.5	30.10	—	80.5°
29.80	71.5	89.0	40.00	—	83.0
40.11	76.0	91.5	49.89	—	85.5
49.90	77.0	94.5	60.12	—	91.5
60.00	75.0	98.5	70.08	—	98.5
70.07	70.5	103.0	80.00	—	110.5
80.14	—	111.0	90.00	—	124.5
89.90	—	121.5			
Section 2: 20% ethanol, 80% water			Section 4: 60% ethanol, 40% water		
9.63	—	79.0°	49.85	—	63.0°
20.10	—	84.0	60.07	—	78.0
30.00	—	85.5	70.13	—	92.5
40.13	67.0°	86.0	80.00	—	106.5
50.00	75.0	88.5	90.00	—	123.5
60.00	68.0	93.0			
70.11	—	100.0	Section 5: 80% ethanol, 20% water		
79.00	—	108.0			
89.92	—	120.5	50.0	—	66.0°
			60.06	—	80.0
			70.00	—	93.5
			80.00	—	108.0
			89.05	—	124.0

Figure 1 shows that the stratification curves of all sections (as in the binary system anthranilic acid–water) lie under the crystallization curves of the acid. Hence, the entire stratification surface of the ternary system lies under the crystallization surface of anthranilic acid. Thus the entire stratification volume of the ternary system is a volume of metastable liquid-phase equilibrium.

Five solubility isotherms of the ternary system anthranilic acid – water – ethanol were constructed from the polytherms obtained: stratification isotherms at 70, 75, and 77° and crystallization isotherms at 80 and 85° (Fig. 2). The stratification isotherms clearly show that the volume of the two-phase liquid state adjoins the side of the binary system and lies along it. Therefore, the upper point of this volume is the critical point C of the indicated binary system at 78°. From Fig. 2, it is evident that the stratification volume is very narrow, and extends only up to a content of 13-15% ethanol in the mixtures, in the prism of the ternary system. Thus, ethanol is a very powerful homogenizer of stratification in the binary system anthranilic acid – water.

The crystallization isotherms for solid anthranilic acid in water – ethanol mixtures have solubility maxima. It is of interest that these maxima occur in the binary system water – ethanol at a molar ratio of about 1 : 1 between the components, as in the ternary system with salicylic acid. Therefore, the binary system water–ethanol is a solvent system [6] with respect to anthranilic acid.

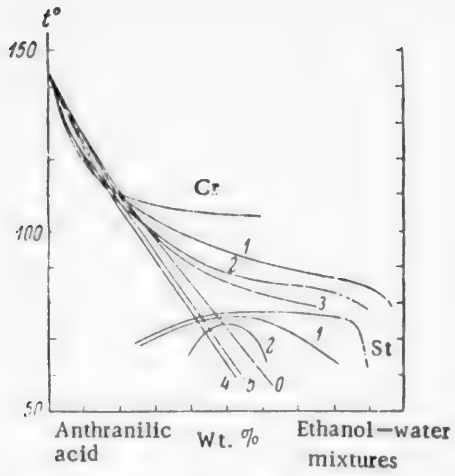

Fig. 1. Polytherms of the ternary system anthranilic acid – water – ethanol. a) Crystallization curve of the system anthranilic acid – ethanol; Cr and St are crystallization and stratification curves, respectively, of the system anthranilic acid – water. Ethanol content in ethanol – water mixtures (in %): 1) 10; 2) 20; 3) 40; 4) 60; 5) 80.

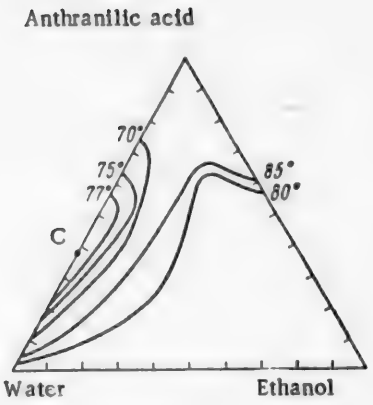

Fig. 2. Solubility isotherms of the ternary system anthranilic acid – – water – ethanol. C is the critical point of the system anthranilic acid – water.

SUMMARY

1. The ternary system anthranilic acid – water – – ethanol was studied with regard to stratification and melting point. It was found to be a ternary system with one narrow volume of metastable equilibrium between liquid phases, adjoining the plane of the binary system anthranilic acid – water.

2. It was shown that the binary system water – ethanol is a solvent system for anthranilic acid.

LITERATURE CITED

1. I. L. Krupatkin, Zhur. Obshch. Khim., Collection I, 151 (1953).
2. Flaschner and Rankin, Monatsh. 31, 23 (1910).
3. V. F. Alekseev, Zhur. Russ. Fiz.-Khim. Obshchestva 8, 249 (1876).
4. I. F. Shreder, Gornyi Zhur., No. 11 (1890).
5. I. L. Krupatkin, Zhur. Obshch. Khim. 26, 1831 (1956).*
6. R. V. Mertslin and V. D. Vasev, Zhur. Obshch. Khim. 21, 417 (1951).*

* Original Russian pagination. See C. B. translation.

PHYSICOCHEMICAL INVESTIGATION OF SOLUTIONS OF CERTAIN MONATOMIC ALCOHOLS IN ACETONE

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The densities, viscosities, latent heats of vaporization, and critical temperatures of monatomic alcohols [1-4] and their solutions in water and monocarboxylic acids [5] were studied earlier. The purpose of the present investigation was to study the viscosity, density, latent heat of vaporization, and critical temperature of solutions of methanol, ethanol, propanol, and butanol in acetone. Some graphical data on the main results of investigation of these solutions are given in [6]. Investigation of molecular light scattering showed that these solutions belong to the molecular-mixed type [7].

EXPERIMENTAL

The substances used in the work were carefully purified. The methanol, ethanol, propanol, and butanol were dried over metallic calcium and distilled through a rectification column, the fractions boiling at 64.6, 78.3, 97-97.4, and 117.2-117.7°, respectively, being collected in this case.

The acetone was refluxed in a flask with potassium permanganate for 4-5 hours. The distilled acetone was kept over fresh anhydrous calcium chloride and distilled over $CaCl_2$, the fraction boiling at 56° being collected.

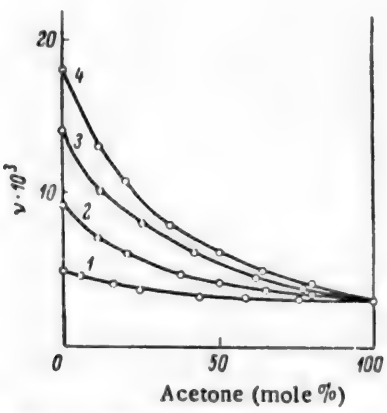

Fig. 1. Viscosity isotherms of solutions of methanol (1), ethanol (2), propanol (3), and butanol (4) in acetone.

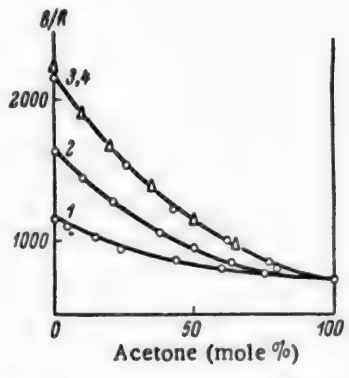

Fig. 2. Concentration dependence of the activation energy for viscous flow of solutions of methanol (1), ethanol (2), propanol (3), and butanol (4) in acetone.

The viscosity measurements were carried out in a closed capillary viscosimeter, described earlier [1]. The viscosity was investigated in a broad temperature interval, from 25 to 90°. The critical temperature of the solutions was determined through the disappearance of the meniscus. Results of the viscosity and critical-temperature measurements are given in Table 1, and viscosity isotherms at 50°, in Fig. 1. The temperature-dependence curves of solutions of alcohols in acetone lie between the curves of the components, and are located higher, the higher the critical temperature of the solution.

In all cases considered, the temperature dependence of viscosity follows an exponential law. The concentration dependence of the activation energy for viscous flow is shown in Fig. 2.

TABLE 1

Viscosity (ν) and Critical Temperature of Solutions of Monatomic Alcohols in Acetone

Acetone concentration (mole %)	$\nu \cdot 10^3$ (in stokes)				Critical temperature
	25°	50°	70°	90°	
Solutions of methanol in acetone					
0.00	6.90	5.12	4.15	3.47	240.7°
5.10	6.46	4.84	3.93	3.30	239.0
15.24	5.68	4.34	3.60	3.04	237.0
24.39	5.00	3.90	3.28	2.85	234.5
44.30	4.48	3.57	3.04	2.65	234.0
59.04	4.21	3.42	2.95	2.62	234.0
76.31	3.98	3.29	2.87	2.55	234.0
100.0	3.90	3.23	2.83	2.51	235.5
Solutions of ethanol in acetone					
0.00	14.10	9.34	6.86	5.50	241.0
10.54	10.24	7.14	5.50	4.39	240.5
20.58	8.50	6.09	4.82	3.93	240.0
37.60	6.33	4.89	3.97	3.34	238.0
50.29	5.44	4.22	3.56	3.07	237.5
64.65	4.73	3.78	3.25	2.86	236.8
79.50	4.29	3.49	3.02	2.64	235.7
Solutions of propanol in acetone					
0.00	25.20	14.18	9.73	6.98	263.0
10.63	18.24	11.14	7.98	5.94	260.7
26.19	12.17	8.01	6.13	4.82	257.0
43.40	9.31	6.67	5.21	4.23	253.7
62.38	5.99	4.59	3.84	3.27	250.0
77.67	4.88	3.98	3.34	2.93	244.0
Solutions of butanol in acetone					
0.00	31.69	18.00	12.04	8.51	287.0
10.39	21.15	13.01	9.29	6.94	284.0
19.19	16.89	10.87	8.03	6.16	282.0
34.80	11.41	7.91	6.15	4.96	274.5
50.29	8.20	6.07	4.90	4.06	269.5
64.93	6.32	4.87	4.06	3.49	258.0
78.91	4.98	4.00	3.45	3.00	251.0

The activation energy is a quadratic function of the concentration; i.e., it is described by the equation

$$B = U_{11}C_1^2 + 2U_{12} \cdot C_1C_2 + U_{22}C_2^2 = \alpha C_1^2 + \beta C_1 + \gamma, \qquad (1)$$

where B is the activation energy, C is the concentration, and U is the energy of interaction between molecules: of the alcohol [U_{11}], acetone [U_{22}], and different types [U_{12}]; $\alpha = U_{11} + U_{22} - 2U_{12}$; $\beta = 2(U_{12} - U_{22})$.

Numerical values of the coefficients α, β, and γ and values of U_{11}, U_{22}, and U_{12}, calculated from them, are given in Table 2.

TABLE 2

Solution	α	β	γ	U_{11} (kcal/mole)	U_{22} (kcal/mole)	U_{12} (kcal/mole)
Methanol–acetone	0.493	0.258	1.45	2.29	1.45	1.58
Ethanol–acetone	1.61	0.844	1.45	3.26	1.45	1.49
Propanol–acetone	2.20	0.655	1.45	4.27	1.45	1.78
Butanol–acetone	1.89	0.811	1.45	4.45	1.45	1.86

TABLE 3

Density (d_4^t) of Solutions of Monatomic Alcohols in Acetone

Acetone conc. (wt. %)	Temperature			
	30°	50°	70°	90°
Solutions of methanol in acetone				
0.00	0.782	0.763	0.743	0.723
8.91	0.790	0.776	0.758	0.735
24.89	0.787	0.766	0.745	0.723
43.44	0.787	0.766	0.743	0.721
61.11	0.786	0.764	0.741	0.718
72.30	0.784	0.760	0.737	0.715
Solutions of ethanol in acetone				
0.00	0.781	0.763	0.744	0.725
13.66	0.783	0.765	0.746	0.726
24.63	0.782	0.762	0.742	0.721
43.18	0.783	0.762	0.740	0.719
56.04	0.782	0.760	0.738	0.717
69.76	0.783	0.760	0.736	0.715
83.03	0.781	0.758	0.734	0.712
Solutions of propanol in acetone				
0.00	0.799	0.781	0.763	0.744
9.37	0.797	0.779	0.761	0.742
22.62	0.794	0.775	0.756	0.735
31.82	0.792	0.772	0.752	0.730
52.60	0.789	0.768	0.746	0.723
65.60	0.787	0.764	0.741	0.719
76.81	0.784	0.761	0.738	0.716
Solutions of butanol in acetone				
0.00	0.803	0.787	0.770	0.752
8.32	0.800	0.784	0.766	0.748
15.68	0.800	0.782	0.764	0.745
29.48	0.796	0.777	0.758	0.738
44.22	0.792	0.772	0.752	0.731
59.20	0.789	0.768	0.747	0.725
75.60	0.785	0.763	0.741	0.718

As follows from the data obtained, the energy of interaction between molecules of alcohols and acetone is less than between molecules of alcohols, but greater than between acetone molecules. This is confirmed by the results of thermodynamic calculations of these quantities [8].

The density of the solutions was determined by the float method [2], based on fixing of the position of neutral equilibrium of a glass float in the liquid under investigation; the float was graduated beforehand in another liquid, of known density. The error of density measurement by this method is about 0.1%. Results of the density measurements are given in Table 3.

In characterizing the volumetric properties of the solutions it is of interest to consider the temperature and concentration dependence of the apparent molar volume of the substance. If the true molar volume of the dissolved substance is subtracted from the latter, the resulting difference is determined by the interaction of the dissolved substance and the solvent, and therefore is of considerable interest. We calculated the apparent molar volumes of acetone dissolved in alcohols at 30 and 70° (Fig. 3). In methanol and ethanol a certain decrease in the apparent molar volume of acetone is observed only at high concentrations of the alcohol, whereas in propanol and butanol the acetone molecule does not contract. The degree of contraction also is unaffected by an increase in temperature. The contraction of acetone is apparently determined both by the amount of change in the free volume of the solvent and by the extent of intermolecular interaction occurring in the solution.

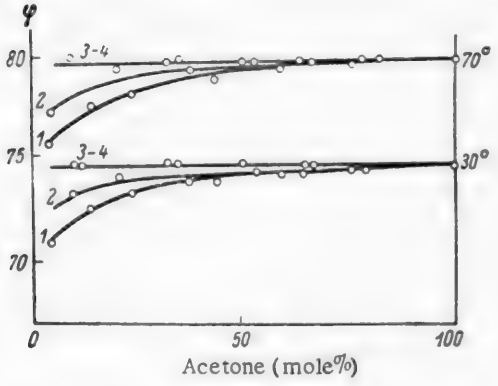

Fig. 3. Concentration dependence of the apparent molar volume of acetone dissolved in methanol (1), ethanol (2), propanol (3), and butanol (4).

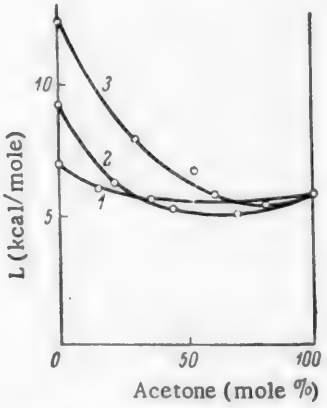

Fig. 4. Isotherms of the latent heat of vaporization of solutions of methanol (1), ethanol (2), and butanol (3) in acetone at 40°.

TABLE 4

Latent Heat of Vaporization (L) of Solutions of Monatomic Alcohols in Acetone at 40°

Methanol–acetone system		Ethanol–acetone system		Butanol – acetone system	
acetone, mole %	L (kcal/M)	acetone, mole %	L (kcal/M)	acetone, mole %	L (kcal/M)
0.0	6.7	0.00	9.0	0.00	12.4
15.89	5.9	21.51	6.0	30.04	7.7
35.39	5.5	43.89	5.3	53.15	6.7
60.91	5.6	69.87	4.9	80.87	5.3
100.0	5.7		—	—	—

The latent heat of vaporization, being a quantity directly related to intermolecular interaction in liquids, can give valuable information on processes occurring in solutions. The latent heat of vaporization was measured by a compensation micromethod [9]. The error of measurement did not exceed 5%. The results of heat-of-vaporization measurements, given in Table 4 and Fig. 4, show that the isotherms are convex with respect to the composition axis.

This indicates that the extent of interaction between molecules of acetone and an alcohol is less than between alcohol molecules. Actually, as was shown by the optical investigations of Malyshev [10], two types of bonds must be distinguished in pure alcohols: the hydrogen bond and the stronger hydroxyl bond. On dilution of the alcohol with acetone the probability of favorable orientation for the formation of a hydroxyl bond between alcohol molecules decreases, and the weaker hydrogen bonds, formed both between molecules of different kinds and between alcohol molecules, predominate in the solution. Corresponding to this, the latent heat of vaporization of the solution at high acetone concentrations is less than the latent heat for the pure components. This also agrees with the results of viscosity measurements set forth above.

SUMMARY

1. The viscosity, density, critical temperatures, and latent heat of vaporization of solutions of methanol, ethanol, propanol, and butanol in acetone were studied.

2. On the basis of a study of the concentration dependence of activation energy for viscous flow and certain calculations, it was shown that the interaction between molecules of alcohols and acetone is weaker than the interaction between alcohol molecules but more pronounced than that between acetone molecules.

3. Study of solution densities in a wide temperature and concentration interval made it possible to evaluate the contraction of acetone in the solutions.

4. Data on the latent heat of vaporization of the solutions are in accord with the results of viscosity measurements with respect to the character of interaction in the solutions.

LITERATURE CITED

1. A. Z. Golik, S. D. Ravikovich, and A. V. Orishchenko, Ukrain. Khim. Zhur. 17, 627 (1951).
2. A. Z. Golik, S. D. Ravikovich, and A. V. Orishchenko, Ukrain. Khim. Zhur. 21, 167 (1955).
3. A. Z. Golik and S. D. Ravikovich, Doklady Akad. Nauk Ukr. SSR 101, 2 (1950).
4. A. Z. Golik and S. D. Ravikovich, Zhur. Fiz. Khim. 23, 86 (1949).
5. V. P. Solomko, Dissertation (Kiev, 1954) [in Russian].
6. A. Z. Golik and R. F. Mocharnyuk, Ukrain. Khim. Zhur. 24, 29 (1958).
7. G. P. Roshchina, Ukrain. Fiz. Zhur. 1, 183 (1956).
8. J. A. Barker and F. Smith, J. Chem. Phys. 22, 375 (1954).
9. A. Z. Golik, S. D. Ravikovich, V. P. Solomko, and Yu. I. Shimanskii, Doklady Akad. Nauk UkrSSR 21, 170 (1955).
10. V. I. Malyshev, Uspekhi Fiz. Nauk 63, 323 (1957).

PHYSICOCHEMICAL INVESTIGATIONS OF SOLUTIONS OF CERTAIN ACIDS OF THE ALIPHATIC SERIES IN ACETONE

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Electron-diffraction and optical investigations [1, 2], and also a study of the molar polarization [3] of solutions of acids in various solvents, indicate the presence of dimeric forms of the acids. These dimeric forms are stable, as is confirmed by their existence in the gas phase at temperatures up to 200°.

As the investigations of Davis [4] showed, in some solvents the bond energy of the acid dimers depends to a considerable extent on the dielectric constant of the solvent. As a result of this, the dimers may be completely dissociated at appreciable dilutions in a solvent with a high dielectric constant. Hence, for instance, in solutions in acetone, which has a relatively high dielectric constant, one can expect a rather complex picture of the structure, depending to a considerable degree on the acetone concentration. Roshchina [5] investigated molecular light scattering in solutions of acetic, butyric, and caproic acids in acetone. In works [6, 7] the viscosity of certain systems, consisting of ketones and organic acids, was investigated.

In the present work the viscosity, density, critical temperature, and latent heat of vaporization of solutions of formic, acetic, propionic, butyric, and caproic acids in acetone were studied. Some graphical data on these solutions were published earlier [8].

EXPERIMENTAL

The starting materials were carefully purified. C. P.* grade formic and acetic acids were purified by multiple fractional freezing. In this way acids with m. p.'s 8.5 and 16.2° were obtained. Propionic, butyric, and caproic acids were distilled three times, the fractions boiling at 140-141°, 163-164°, and 204.5-205° being collected. Acetone purification and the experimental procedure were described earlier [9].

Viscosity and density were studied in the temperature interval 25-90° and the latent heat of vaporization, at 40°. The results of viscosity and critical-temperature measurements are given in Table 1, whereas the viscosity isotherms at 50° for all five systems are shown in Fig. 1. As in the case of solutions of alcohols in acetone, the curves of the temperature dependence of viscosity of these solutions lie between the corresponding curves for pure components and in the order of increase of their critical temperatures.

In all solutions of acids in acetone, which we investigated, the temperature dependence of viscosity closely follows an exponential law; this made it possible to study the character of the concentration dependence of the activation energy for viscous flow (B). The curves shown in Fig. 2 do not follow a square law; in view of this, the energy of interaction between acid and acetone molecules could not be calculated.

The activation energy for viscous flow of solutions increases with their critical temperature.

Results of solution-density measurements are given in Table 2.

*Chemically pure.

TABLE 1

Viscosity and Critical Temperature of Solutions of Fatty Acids in Acetone

Acetone conc. (mole %)	$\nu \cdot 10^3$ (in stokes)				Critical temperature
	25°	50°	70°	90°	
Solutions of formic acid in acetone*					
0.00	12.62	8.75	6.7	5.37	
11.54	11.26	7.75	6.07	4.95	
28.14	8.82	6.43	5.20	4.32	
44.84	7.40	5.58	4.61	3.91	
55.38	6.24	4.84	4.07	3.48	
72.24	5.11	4.09	3.50	3.06	
100.0	3.90	3.23	2.83	2.51	
Solutions of acetic acid in acetone					
0.00	10.41	7.67	6.13	5.16	321.0°
10.28	9.78	7.15	5.83	4.49	311.5
17.23	9.44	6.97	5.66	4.73	308.0
29.47	8.26	6.30	5.16	4.35	296.8
45.85	6.95	5.35	4.44	3.82	288.5
66.03	5.83	4.59	3.90	3.39	274.0
81.44	4.77	3.86	3.33	2.94	257.5
100.0	3.90	3.23	2.83	2.51	235.5
Solutions of propionic acid in acetone					
0.00	10.61	7.85	6.38	—	327.8
9.96	10.09	7.56	6.21	5.22	318.5
22.70	9.27	7.00	5.77	4.88	312.0
39.44	8.06	6.15	5.12	4.38	300.5
57.56	6.68	5.22	4.42	3.83	288.5
76.71	5.32	4.28	3.67	3.22	269.5
100.0	3.90	3.23	2.83	2.51	235.5
Solutions of butyric acid in acetone					
0.00	16.18	11.15	8.87	7.18	339.0
14.54	13.88	9.88	7.87	6.47	333.0
30.55	11.62	8.46	6.89	5.73	326.0
39.23	10.49	7.70	6.27	5.23	316.0
48.90	9.29	6.97	5.76	4.86	311.0
50.03	8.25	6.27	5.22	4.44	302.5
70.48	6.65	5.17	4.40	3.77	285.0
72.68	5.73	4.57	3.90	3.41	272.6
89.51	4.69	3.80	3.29	2.92	257.6
Solutions of caproic acid in acetone					
0.00	30.92	19.22	14.38	11.15	369.8
24.81	20.62	13.87	10.68	8.59	361.0
39.50	16.17	11.25	8.86	7.22	—
44.83	14.47	10.22	8.17	6.70	352.0
60.37	10.50	7.77	6.36	5.32	325.8
72.24	8.35	6.33	5.28	4.49	306.8
80.95	6.48	5.09	4.32	3.73	294.0

* The critical temperatures of solutions of formic acid in acetone were not measured, since formic acid decomposes.

TABLE 2

Density of Solutions of Fatty Acids in Acetone

Acetone conc. (mole %)	d_4^t			
	30°	50°	70°	90°
Solutions of formic acid in acetone				
0.00	1.205	1.180	1.154	1.129
13.14	1.110	1.092	1.069	1.047
32.40	1.027	1.000	0.977	0.953
46.00	0.967	0.945	0.920	0.897
61.03	0.911	0.887	0.863	0.839
77.36	0.853	0.830	0.807	0.783
100.0	0.779	0.756	0.731	—
Solutions of acetic acid in acetone				
0.00	1.039	1.017	0.995	0.972
9.98	1.011	0.989	0.966	0.944
16.57	0.993	0.976	0.953	0.930
28.78	0.956	0.935	0.912	0.888
45.10	0.915	0.891	0.868	0.845
62.49	0.871	0.848	0.825	0.802
80.98	0.825	0.803	0.779	0.754
Solutions of propionic acid in acetone				
0.00	0.985	0.964	0.943	0.922
12.19	0.959	0.938	0.917	0.895
30.20	0.904	0.882	0.860	0.838
43.18	0.880	0.858	0.836	0.815
61.76	0.846	0.823	0.802	0.777
72.12	0.835	0.813	0.790	0.766
85.63	0.814	0.791	0.767	0.743
Solutions of butyric acid in acetone				
0.00	0.949	0.930	0.910	0.889
10.16	0.932	0.911	0.892	0.871
22.48	0.910	0.890	0.871	0.849
29.85	0.899	0.878	0.858	0.837
38.68	0.884	0.863	0.842	0.822
45.65	0.872	0.851	0.829	0.809
61.15	0.846	0.825	0.803	0.781
Solutions of caproic acid in acetone				
0.00	0.921	0.903	0.885	0.867
14.16	0.912	0.894	0.876	0.858
28.89	0.892	0.876	0.854	0.835
33.70	0.885	0.867	0.848	0.829
48.60	0.859	0.840	0.819	0.801
56.53	0.844	0.824	0.805	0.783
67.99	0.825	0.805	0.783	0.761

We calculated the apparent molar volumes of acetone (φ) dissolved in acids at 30 and 70° (Fig. 3). In acids considerable contraction of acetone is observed, which increases with the order of the acid and its concentration, and also on increase of temperature.

It is of great interest to know the latent heat of vaporization of the solutions, since this quantity characterizes the intermolecular interaction. The latent heat of vaporization was studied at 40° (Table 3, Fig. 4).

Isotherms of this property are rather complex in form. In considering them the relatively complex structure of fatty acids must be taken into account.

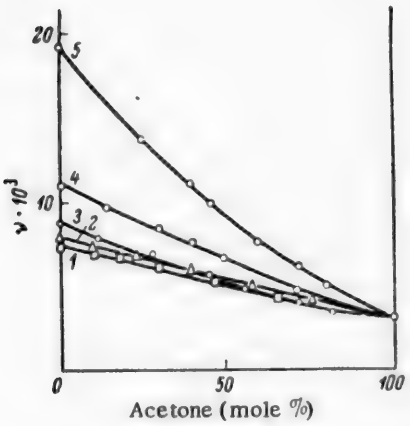

Fig. 1. Viscosity isotherms of solutions of propionic (1), acetic (2), formic (3), butyric (4), and caproic (5) acids in acetone.

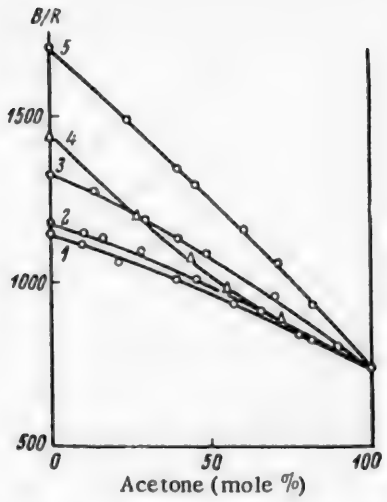

Fig. 2. Concentration dependence of the activation energy for viscous flow of solutions of propionic (1), acetic (2), butyric (3), formic (4), and caproic (5) acids in acetone.

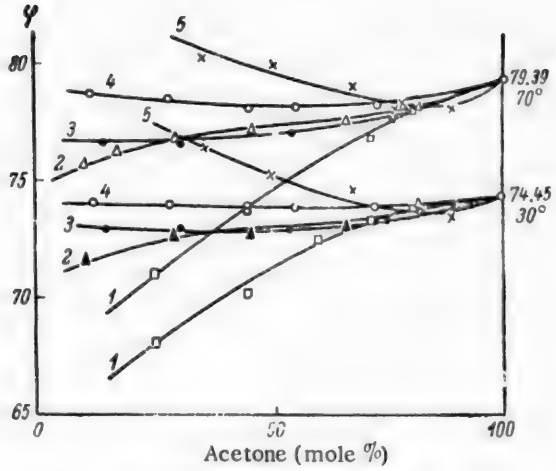

Fig. 3. Concentration dependence of the apparent molar volume of acetone dissolved in caproic (1), acetic (2), butyric (3), formic (4), and propionic (5) acids.

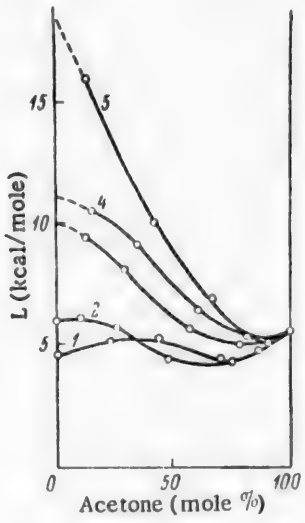

Fig. 4. Isotherms of the latent heat of vaporization of solutions of formic (1), acetic (2), propionic (3), butyric (4), and caproic (5) acids in acetone.

As indicated above, the dimers of the acids are very stable and do not dissociate even on vaporization. The bond energy of the dimer molecules is about 14 kcal/mole. However, as investigations by certain authors [4] showed, the bond energy of the dimeric ring is sharply decreased in solution – the greater, the higher is the dielectric constant of the solvent. For instance, in solutions in chlorobenzene, whose dielectric constant is 6, the enthalpy change ΔH_2^0 of the acid dimer, which characterizes the interaction energy, is equal to 5 kcal/mole, i.e., of the order of energy of hydrogen bonds in alcohols. When acetic acid is dissolved in water, the dimeric rings are broken; in a 10% solution the dimer is practically fully dissociated as a result of the formation of chain

complexes based on the hydrogen bond between water and acetic acid molecules [10]. It is possible that in very dilute solutions of acids in acetone, whose dielectric constant is 21, the bonds of a certain part of the dimeric rings are completely cleaved, and monomeric forms appear along with the dimeric ones in the solutions.

TABLE 3

Latent Heat of Vaporization (L) of Solutions of Fatty Acids in Acetone

Formic acid–acetone		Acetic acid–acetone		Propionic acid–acetone		Butyric acid–acetone		Caproic acid–acetone	
mole %	L (kcal/M)	mole %	L (kcal/M)	mole %	L (kcal/M)	mole %	L (kcal/M)	mole %	L (kcal/M)
0.00	4.6	0.00	5.5	0.00	10.5*	0.00	11.8*	0.00	18.5*
21.73	5.3	10.41	6.3	12.65	9.6	14.6	10.6	12.31	16.0
44.21	5.4	25.81	5.9	27.7	8.3	33.9	9.3	40.38	9.9
71.0	4.5	50.5	4.6	56.25	5.8	59.79	6.5	67.17	7.4
—	—	75.08	4.4	79.32	5.1	78.71	5.5	85.61	4.9
100	5.7	—	—	—	—	—	—	—	—

* Data obtained by extrapolation.

The existence of monomeric and dimeric forms in the solutions is also reflected in the character of the isotherms of the latent heat of vaporization. For solutions of acetic and formic acids in acetone they are concave with respect to the composition axis at high acid concentrations. When the acetone content is high, a pronounced minimum is observed. These considerations are confirmed also by investigations of the molar polarization [4] and infrared absorption spectra of solutions of acids in different solvents [11] and by N. A. Izmailov's data on Raman scattering in this system [12]. On passing to higher members of the fatty-acid series the latent-heat isotherms are somewhat smoothed out. Apparently the shape of the isotherms is substantially affected by the great difference in the heats of vaporization of the solution components.

SUMMARY

1. The viscosity, density, critical temperature, and latent heat of vaporization of solutions of formic, acetic, propionic, butyric, and caproic acids in acetone were studied.

2. On the basis of density measurements of solutions and study of the temperature and concentration dependence of the apparent molar volume of acetone in acids, it was established that acetone contracts to a degree increasing with the acid concentration and temperature.

3. The shape of the isotherms of latent heat of vaporization indicates a complex picture of solution structure, which is due to the dissociation of dimeric forms of the acids to monomeric in a solvent with a high dielectric constant.

LITERATURE CITED

1. J. Karle and L. O. Brockway, Proc. Nat. Acad. Sci. 20, 336 (1934).
2. M. I. Batuev, Doklady Akad. Nauk SSSR 52, 405; 53, 321, 511 (1946). H. B. Pohl, M. E. Hobbs, and P. M. Gross, J. Chem. Phys. 9, 408 (1941).
3. A. A. Maryott, M. E. Hobbs, and P. M Gross, J. Am. Chem. Soc. 71, 1671 (1949).
4. M. Davies, P. Jones, D. Patnaik, and E. M. Mollwyn-Hughes, J. Chem. Soc. (1951), p. 1249.
5. G. P. Roshchina, Vestnik KGU, (1958), No. 2.
6. J. Kendall and F. Brakeley, J. Am. Chem. Soc. 43, 1827 (1921); D. Faust, Z. phys. Chem. 79, 97 (1921).
7. V. V. Udovenko, Zhur. Obshch. Khim. 9, 1163, 1564 (1939).

8. A. Z. Golik and R. F. Mocharnyuk, Ukrain. Khim. Zhur. 24, 33 (1958).
9. R. F. Mocharnyuk, Zhur. Obshch. Khim. 30, 1081 (1960).*
10. M. I. Batuev, Izvest. Akad. Nauk SSSR, Ser. Fiz., 12, 612 (1948).
11. R. H. Gillette, J. Am. Chem. Soc. 74, 4151 (1952); L. Kinsey and J. W. Ellis, J. Chem. Phys. 5, 399 (1937).
12. N. A. Izmailov and L. M. Kutsyna, Izvest. Akad. Nauk SSSR, Ser. Fiz., 17, 740 (1953).

*Original Russian pagination. See C. B. translation.

ACIDITY CONSTANTS OF DIASTEREOISOMERIC TETRAHYDROXYADIPIC ACIDS AND THEIR MONOLACTONES

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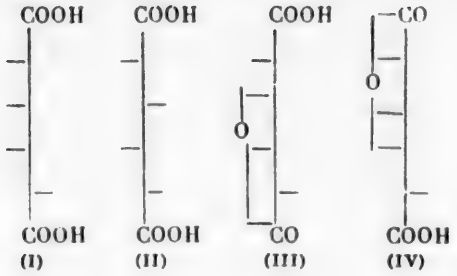
The relation between the acidity of diastereoisomeric tetrahydroxyadipic acids (THAA) and their cyclic derivatives – anhydroacids and monolactones – and the steric configuration of the polyhydroxymethylene chain is of interest in the study of certain characteristic structural peculiarities determining the tendency toward lactone formation, the rate of establishment of acid-lactone equilibrium, the ability to form Δ^{α}-butenolides, etc. The acidity of THAA and their 2,5-anhydro derivatives was systematically investigated at one time by Levene and Simms [1]. Values of the dissociation indices (pK_1) measured by them for D-glucosaccharic, mucic, and DL-talomucic acids* are very close to each other, being equal to 3.34 ± 0.06 (the somewhat lower value of pK_1 for D-mannosaccharic acid, according to the authors' data, is unreliable). The acidity of 2,5-anhydro-THAA proved to be much higher than that of the THAA themselves: the pK_1 of 2,5-anhydroacids with the 2,5-OH groups in the cis-position (gluco, gala) is about 2.1, whereas the pK_1 of 2,5-anhydroacids with these OH groups in the trans-position (manno, ido) is about 3.0; the difference in the dissociation of the two groups of anhydro-acids may be explained by the difference in the distances between COOH groups in cis- and trans-isomers, due to the steric forms of the molecules [1].

As we showed earlier, closing of the lactone ring of a polyhydroxy-ω-dicarboxylic acid with participation of one COOH group is accompanied by a considerable increase of acidity; on formation of the monoester the dissociation constant decreases 50-60% [4]. In the present work we give our values of the acidity indices for certain THAA and their monolactones, which confirm the regularity mentioned above (table).

Dissociation Indices for Certain Tetrahydroxyadipic Acids and Their Monolactones

Substance	Formula (No.)	pK_1	pK_2	$pK_2 - pK_1$
D-Talomucic acid	(I)	3.45	4.25	0.80
DL-Talomucic acid		3.47	4.29	0.82
D-Idosaccharic acid	(II)	3.26	4.13	0.87
D-Talomucic 3,6-monolactone	(III)	2.84	–	–
D-Talomucic 1,4-monolactone	(IV)	2.81	–	–

* In conformity with the views of that time [2] Levene and Simms incorrectly considered DL-talomucic acid to be allomucic acid. In 1935, it was shown [3] that "allomucic acid," prepared by epimerization of mucic acid, actually is DL-talomucic acid.



(I) (II) (III) (IV)

Thus the order of decreasing acidity in the THAA group is the following: manno > gluco > gala, ido > > talo.

Although the differences among the dissociation indices of diastereoisomeric THAA are very slight, they are appreciable, and on the basis of their order, a hypothesis on the reasons for the unequal acidities of the diastereoisomers may be advanced.

The joint effect of the two COOH end groups, which determines the acidity of n-dicarboxylic acids, both in THAA and adipic acid, is essentially the effect of the electrostatic field produced by one COOH group and the ionizable hydrogen atom of the other COOH group.

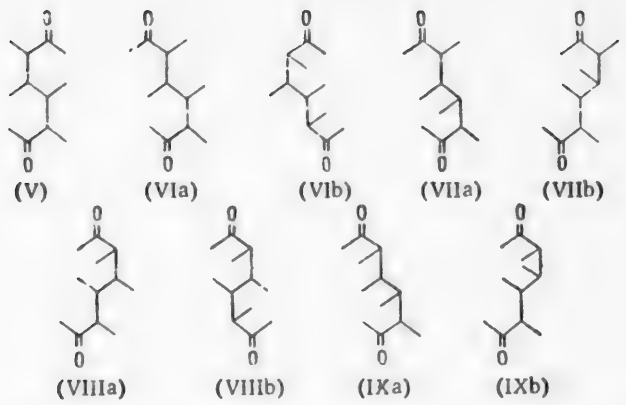
The factors determining the intensity of this joint effect may be: 1) the distance between the COOH groups and 2) the dielectric constant of the intramolecular space between the COOH groups.

The distance between the COOH groups, r (in A), may be calculated by means of the Bjerrum equation [5], $pK_2 - pK_1 = \frac{B}{Dr} + 0.6$, where $B = \frac{e^2}{2.303kT} = 243.3$ (at 25°); e is the electronic charge, k is Boltzmann's constant, T is the absolute temperature, D is the dielectric constant, and 0.6 is the logarithm of the statistical factor (equal to 4 in the case of dissociation of a dicarboxylic acid). If, according to Bjerrum's conception, D is considered equal to the dielectric constant of the solvent – water – $B/D = 3.1$. Values of r for THAA, calculated with this condition, vary from 6 to 15.5 A, and the average value of r is 10.9 A, which agrees with the data of Levene and Simms: 8-16 A, average 11.5 A [1]. Until now the structure of THAA molecules has not been studied either in the crystalline state or in solution. Investigation of the crystal structure of potassium and rubidium D-gluconates, which are very similar to THAA, shows that the polyhydroxymethylene chain of gluconic acid has exactly the same type of structure as the plane, zigzag carbon chains of aliphatic n-carboxylic acids, tetrahedral bond angles being maintained [6]. In the adipic acid molecule the distance corresponding to r is – with a rigid chain structure in the crystal lattice – about 6.6 A; this same distance, calculated by the Bjerrum equation, is 7.8 A.* Hence, it is unlikely that values of r for THAA, calculated by the Bjerrum equation (about 11 A), represent any real distances in the molecule.**

Taking into account the ease of cyclization (lactonization) of polyhydroxycarboxylic acids, it is possible that the polyhydroxymethylene chain in these compounds is folded at least partially in the form of a meander and that it contains, as it were, preformed constellations of lactone rings whose closing requires only the splitting-out of a water molecule. Thus, for instance, the structure of D-mannosaccharic acid may be represented by (V), that of D-glucosaccharic acid by (VIa, b), mucic acid by (VIIa, b), D-idosaccharic acid by (VIIIa, b), and D-talomucic acid by (IXa, b); all chain constellations shown below correspond to actually existing γ-lactones.

* The inaccuracy Δr of the value of r, calculated by the Bjerrum equation, for an error $\Delta\delta$ in the difference $pK_2 - pK_1 = \delta$ is $\Delta r = \frac{3.1\Delta\delta}{(\delta - 0.6)^2}$, which amounts to ± 1 A when $\delta = 1$ and $\Delta\delta = 0.05$.

** Owing to the free rotation of the links in the carbon chain in solution, and also the tendency of long (over five atoms) chains to form ball-shaped constellations, the actual distance between the two COOH groups must be even slightly less than the value of r, calculated from a rigid model of the chain.



If such a chain constellation occurs, the distance between COOH groups in polyhydroxy-n-carboxylic acids must be much less than the corresponding distance in n-carboxylic acids; it can be shown that with unchanged C–C interatomic distances r_0 and bond angles ϑ the length of a carbon "zigzag" of n carbon atoms

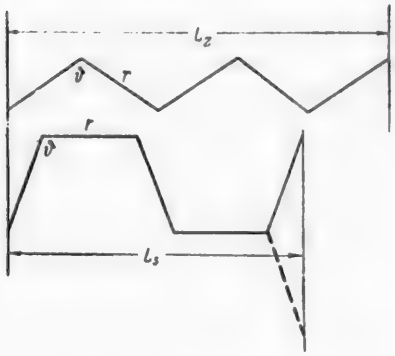
$$L_z = (n-1)\, r_0 \sin\frac{\vartheta}{2}$$

is always greater than the length of the corresponding "meander,"

$$L_s = r_0\left[\left(\frac{n-\sin^2\frac{\pi n}{2}}{2}\right)\sin\left(\vartheta-\frac{\pi}{2}\right)+\left(\frac{n+\sin^2\frac{\pi n}{2}}{2}-1\right)\right],$$

e.g., when n = 6 (THAA), L_z = 6.29 A and L_s = 4.62 A (at r_0 = 1.54 A and ϑ = 109°30') (figure).

In view of what has been set forth above, the hypothesis that the differences in acidity of THAA are due to differences in the true (intramolecular) dielectric constant in the case of molecules of nearly identical geometry (quantities r_0, ϑ, etc.) seems more probable to us. This concept of the dielectric constant corresponds to the "effective" dielectric constant in the Kirkwood-Westheimer model [7, 8].

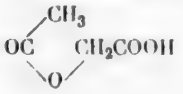


If we assume, in analogy with crystallographically studied compounds containing a tetrahydrofuran ring (L-ascorbic acid, saccharose, cytidine), that all four or at least three carbon atoms, the furan oxygen atom, the lactone oxygen atom, and the OH group are coplanar or nearly so [9], Formulas (V-IX) show appreciable differences in the content of OH groups in the intermolecular space between the COOH groups (in V there are no OH groups between the COOH groups, whereas in IX there are three). The different content of OH groups in the intramolecular space, in our opinion, is the cause of the difference in the effective dielectric constant (which increases with the number of OH groups) and therefore in the strength of the electrostatic field. This explanation agrees well with the order of acidity indices and values of $pK_2 - pK_1$ for THAA. Similarly the higher acidity of 5-nitro-m-2-xylenol in comparison with p-nitrophenol was explained by the lowering of the effective dielectric constant of the intramolecular medium by CH_3 groups [8]. A similar effect possibly causes the considerable difference in acidity between cis- and trans-carbonic (1,1-dimethylcyclopropane-2,3-dicarboxylic) acids (cis-: pK_1 = 2.34; trans- DL: pK_1 = 3.82).

The difference between the acidity indices of D-talomucic and DL-talomucic acids does not exceed the error of measurement; this agrees with the known fact that the acid functions of the racemate differ very slightly or not at all from the acid functions of the corresponding enantiostereoisomers. Arabotrihydroxyglutaric acids remain an unexplained exception to this rule (pK_1 for the L-form, 2.88; pK_1 for the DL-form, 3.16) [10].

The higher acidity of polyhydroxy- ω-dicarboxylic monolactones in comparison with the free acids is apparently due to the "short-circuiting" of both the free and the lactonized COOH groups through the ester oxygen atom. A similar effect is observed in the case of glycolic and O-acetylglycolic acids.

$HOCH_2COOH$ $pK = 3.82$ [11]

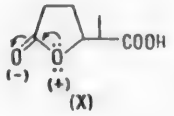


$pK = 2.91$ [12]

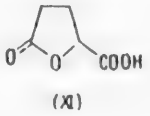
It is generally known that the acetylation of malic acid increases its dissociation constant fivefold [13]. We encounter similar phenomena in the case of 2,5-anhydro-THAA (the pK_1 of isosaccharic acid is 2.08 [1]), thiocarbamylglycolic acid $H_2NCS - O - CH_2COOH$ (pK = 2.95), diglycolic acid, N-acylglycines, etc.

It may be assumed that the O-acyl and lactone groupings affect the dissociation of the COOH group as a result of displacement of electron density toward the CO group (X). This effect must be even more pronounced in α-hydroxyglutarolactone (XI), in the molecule of which the distance between the dipole and the COOH group is less than in tetrahydroxyadipic monolactones.

The occurrence of this electron shift in lactones and cyclic anhydrides is confirmed, in particular, by the considerable dipole moments [14]



(X)



(XI)

EXPERIMENTAL

D-Talomucic acid (I) and its monolactones (III, IV) were prepared from D-talonic acid by a route described in [15]. D-Talonic acid was prepared through the epimerization of D-galactonic acid by aqueous pyridine [16]; the latter acid was prepared by oxidizing D-galactose with bromine in the presence of calcium carbonate [17].

(I): m. p. 153-156° (water), $[\alpha]^{18}D$ + 30.70° (c 2.00, water); (III) (monohydrate): m. p. 63-68° (not sharp) (ethyl acetate) $[\alpha]^{19}D$ + 33.80° (c 2.22, water); (IV): m. p. 185-186° (decomp.) (precipitated from a highly concentrated aqueous solution with acetone), $[\alpha]^{18}D$ + 49.90° (c 2.22, water).

DL-Talomucic acid was prepared by refluxing mucic acid with 10% aqueous pyridine in a round-bottom flask in an oil bath (130-135°) for 48 hours; the product was isolated according to Butler and Gretcher [18]. After two recrystallizations from water, activated charcoal being added, m. p. 172-174° (with gas evolution).

D-Idosaccharic acid (II) was synthesized from D-idonic acid [19] through its dibenzal derivative [20]. The latter was isolated directly from the D-gulonolactone mother liquor. 2,4,3,5-Dibenzylidene-D-idonic acid, m. p. 225-230° (after reprecipitation from solution in KOH and recrystallization from methanol), was converted by oxidation with alkaline permanganate solution by a generally known method [21] to 2,4,3,5-dibenzylidene-D-idosaccharic acid; on hydrolysis with 2% sulfuric acid, the latter gave (II), which was purified by a known method [21]; m. p. 148-150° (acetone).

Values of pK were determined by an approximate electrometric method [4]. Ionic strength of solutions 0.01-0.03, temperature 23 ± 2°. Maximum error ± 0.05 pK unit.

SUMMARY

1. The dissociation constants of D-talomucic, DL-talomucic, and D-idosaccharic acids, as well as D-talomucic monolactones, were determined by an approximate electrometric method.

2. Differences in the acidity of diastereoisomeric tetrahydroxyadipic acids may be explained by differences in the dielectric constant of the intramolecular space between the COOH groups.

LITERATURE CITED

1. P. A. Levene and H. S. Simms, J. Biol. Chem. 63, 351 (1925).
2. E. Fischer, Ber. 24, 2136, 2683 (1891).
3. T. Posternak, Helv. Chim. Acta 18, 1283 (1935).
4. L. A. Mai, Zhur. Obshch. Khim. 26, 3206 (1956).*
5. N. Bjerrum, Z. Phys. Chem. 106, 219 (1923).
6. C. D. Littleton, Acta Cryst. 6, 775 (1953).
7. J. G. Kirkwood and F. H. Westheimer, J. Chem. Phys. 6, 506 (1938).
8. F. H. Westheimer and M. W. Shookhoff, J. Am. Chem. Soc. 61, 555 (1939).
9. A. I. Kitaigorodskii, Organic Crystal Chemistry [In Russian] (Izd. AN SSSR, 1955).
10. O. Ruff and W. Roth, Ber. 32, 559 (1899).
11. W. Ostwald, Z. Phys. Chem. 3, 183 (1889).
12. B. Holmberg, Z. Phys. Chem. 84, 455 (1913).
13. B. Holmberg, Ber. 45, 3003 (1912).
14. L.–B. T., (1951), 6th edition, Vol. I, Pt. III, pp. 419, 422, 428.
15. M. Steiger and T. Reichstein, Helv. Chim. Acta 19, 195 (1936).
16. W. Bosshard, Helv. Chim. Acta 18, 482 (1935).
17. G. H. A. Clowes and B. Tollens, Lieb. Ann. 310, 166 (1900).
18. C. L. Butler and L. H. Cretcher, J. Chem. Soc. (1929), p. 2168.
19. E. Fischer and I. W. Fay, Ber. 28, 1975 (1895).
20. W. A. van Ekenstein and J. J. Blanksma, Rec. Trav. Chim. 27, 1 (1908); Zbl., (1908), I, p. 719.
21. E. Seebeck, E. Sorkin, and T. Reichstein, Helv. Chim. Acta 28, 934 (1945).

* Original Russian pagination. See C. B. translation.

KINETICS OF THE FORMATION AND HYDROLYSIS OF D-MANNOSACCHARO-1,4,3,6-DILACTONE

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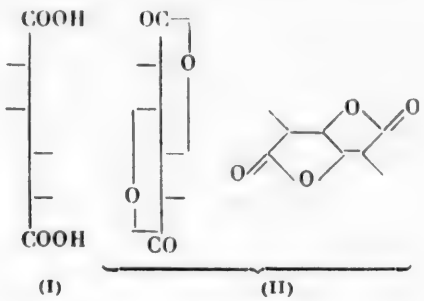
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1097-1099, April, 1960
Original article submitted February 9, 1959

A characteristic peculiarity of D- and L-mannosaccharic acids, their ability to form dilactones, is not possessed by any other diastereoisomeric tetrahydroxyadipic acid* (D-glucosaccharo-γ,δ-dilactone is formed only under relatively severe conditions [3]). This property of mannosaccharic acids, together with the ease of the unique conversion of their dilactones in an alkaline medium, due to the formation of a strongly reducing Δ^{α}-butenolide, at one time even led E. Fischer to doubt the correctness of the established structural formula [4].

By studying the mutarotation of D-glucosaccharic and D-talomucic acids and their monolactones, we found very appreciable differences in the rate constants of formation and hydrolysis of the monolactones of these diastereoisomeric acids [5]. It was of interest to us to find out whether any distinctive peculiarity exists in the kinetics of lactonization of D-mannosaccharic acid (I) and formation of its dilactone (II).



(I) (II)

The change in the specific rotation of (I) and (II) with time – up to 27 days – was studied by Rehorst [6], whose data are in good accord with our polarimetric data.

The rate constant of hydrolysis of the dilactone, K_1, and the rate constant of lactonization of the acid, K_2 [hr^{-1}], were calculated from polarimetric data by means of equations given earlier [5].

Lactonization and hydrolysis curves are shown in the figure.

On comparison of the rate constants of formation and hydrolysis of the D-mannosaccharodilactone with the corresponding constants for D-glucosaccharic and D-talomucic monolactones [5] it is evident that they all have the same order of magnitude: $K_1 = 1.9 - 6.5 \cdot 10^{-3}$, and $K_2 = 1.4 - 7.0 \cdot 10^{-3}$ (hr^{-1}). The kinetics of formation

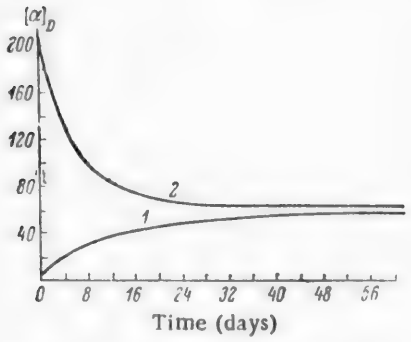
* E. Fischer observed specific rotations of the order of + and – 100° for sirupy preparations of D- and L-idosaccharic acids [1], whereas $[\alpha]^{14}D$ for pure (crystalline) D-idosaccharic acid is equal to + 15.6 ± 3° [2]. Such large shifts of specific rotation can only be due to dilactone formation.

and hydrolysis of D-mannosaccharodilactone thus does not differ substantially, either qualitatively or quantitatively, from the kinetics of formation and hydrolysis of monolactones of other tetrahydroxyadipic acids.

Principal Data on the Kinetics of Formation and Hydrolysis of D-Mannosaccharo-1,4,3,6-Dilactone
(α_0 is the initial specific rotation, α is the specific rotation of the equilibrium mixture, K_1 and K_2 [hr^{-1}])

Initial substance	α_0	α	$K_1 + K_2$	K_1	K_2	$\frac{K_1}{K_2}$
D-Mannosaccharic acid (I)	3.60	56.60	0.00328	—	—	—
D-Mannosaccharo-1,4,3,6-dilactone (II)	203.90	60.60	0.00714	0.00511	0.00203	2.514

The time of establishment of acid–lactone equilibrium for D-glucosaccharic acid is about 20 days, for D-talomucic acid about 60 days, and for D-mannosaccharic acid about 55 days. It must be noted that values of specific rotation and, therefore, compositions of equilibrium mixtures reached from the acid side and from the dilactone side differ appreciably from one another (60.60° and 56.60°); this phenomenon is much less pronounced in the case of D-glucosaccharic and D-talomucic acids. This may be due to some inaccuracy of calculation [5], involving neglect of the concentration dependence of specific rotation, or a more complex reaction mechanism.



Curves of formation and hydrolysis of D-mannosaccharo-1,4,3,6-dilactone. 1) D-Mannosaccharic acid; 2) the dilactone.

It would be interesting to compare the rate constants of formation and hydrolysis of lactones of the tetrahydroxyadipic acids investigated by us with the constants of an idosaccharolactone (or -dilactone). Unfortunately, idosaccharic acids have been little studied until now, and nothing is known of their lactones. The average value of the sum $K_1 + K_2$ for D-idosaccharic acid, calculated by us from polarimetric data for crystalline D-idosaccharic acid [2], is 0.004 and thus is of the same order of magnitude as in the case of all other tetrahydroxyadipic acids (0.003-0.013). Polarimetric investigation of the kinetics of formation and hydrolysis of monolactones of the optically inactive mucic and allomucic acids is possible in principle only in the case of enantiostereoisomeric monolactones, which have not been isolated up to now.

EXPERIMENTAL

D-Mannosaccharo-1,4,3,6-dilactone (II) was prepared by oxidizing D-mannitol with nitric acid at 60° [7], recrystallized twice from ethanol, and dried in vacuo over sulfuric acid; m. p. 186-189°, $[\alpha]^{20}D$ + 203.90° (c 1.1966, water, 10 minutes after solution).

D-Mannosaccharic acid (I) was prepared from the dilactone through the silver salt [6]; m. p. 126-128° (decomp.) (from ethanol), $[\alpha]^{20}D$ + 3.60° (c 2.5000; water, 15 minutes after solution). We described the measurement procedure and calculation earlier [5]. The temperature of measurement and keeping of the solution was 20 ± 2°; c was 2.5000 for (I) and 1.1966 for (II). The value of α_0 for (I) was measured within 15 minutes after solution, and that for (II), within 10 minutes after solution. The measurements were carried out during 58-60 days. Values of the sum $K_1 + K_2$ are the averages of nine measurements; maximum deviations of individual values of this sum did not exceed ± 0.00095 in the case of lactonization of (I), or ± 0.002 in the case of hydrolysis of (II). The arithmetic mean of the $K_1 + K_2$ sums was used for calculation of K_1 and K_2.

SUMMARY

1. The rate constants of formation and hydrolysis of D-mannosaccharo-1,4,3,6-dilactone were determined polarimetrically.

2. The sum of the rate constants of lactone hydrolysis and acid lactonization for D-idosaccharic acid was calculated.

LITERATURE CITED

1. E. Fischer and I. W. Fay, Ber. 28, 1975 (1895).
2. E. Seebeck, E. Sorkin, and T. Reichstein, Helv. Chim. Acta, 28, 934 (1945).
3. K. Rehorst and H. Scholz, Ber. 69, 520 (1936).
4. E. Fischer, Ber. 27, 3228 (1894).
5. L. A. Mal, Zhur. Obshch. Khim. 27, 3192 (1957).*
6. K. Rehorst, Ber. 65, 1476 (1932).
7. R. P. Linstead, L. N. Owen, and R. F. Webb, J. Chem. Soc. (1953), p. 1230.

* Original Russian pagination. See C. B. translation.

SYNTHESIS OF DIENES ON THE BASIS OF OLEFINS AND ALDEHYDES

II. SYNTHESIS OF DIVINYL ON THE BASIS OF PROPYLENE AND FORMALDEHYDE*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1099-1106, April, 1960
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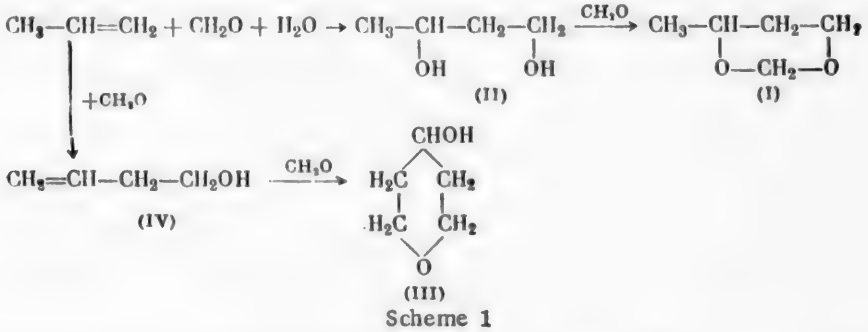
In works published by us earlier [1-3] it was shown that propylene smoothly reacts with formaldehyde in the presence of acid (sulfuric acid concentration 3-5%; temperature 105-115°; pressure 35-45 atm). The main product of this reaction, which is obtained in 80-85% yield reckoned on the formaldehyde consumed, is 4-methyldioxane-1,3 (I). Small amounts of butanediol-1,3 (II) (3-3.5%) and 4-hydroxytetrahydropyran (III) (7-10%) and a trace of allylcarbinol (IV) (about 1%) are obtained at the same time (Scheme 1). We showed [2,4] that (III) is a product of the successive reaction of (IV) with formaldehyde, and gave the mechanism of this reaction



Scheme 1

In the literature there are certain patent declarations, which indicate the possibility of preparing divinyl on the basis of 4-methyldioxane [5], but there is not one experimental work devoted to this question. We investigated in detail the reaction of contact cleavage of methyldioxane (I) in the gas phase over a solid catalyst, which gives divinyl in high yields. Moreover, we showed that under certain conditions, it is possible on this basis to synthesize divinyl and allylcarbinol (IV) simultaneously in approximately equal proportions by weight [6].

Study of the Conditions of Contact Conversion of Methyldioxane. We tried a great number of substances as catalysts for the contact conversion of methyldioxane (I); in this case particular attention was paid to phosphates of various metals. After lengthy study it was found that the best catalyst for this process (as well as isoprene preparation from 4,4-dimethyldioxane [7]) is a mixture of calcium phosphates of a certain composition (KSD catalyst). The chosen catalyst is distinguished by good activity and selectivity, and perfectly satisfactory stability.

* The work was done in the period 1945-1950.

Maximum yields of divinyl are obtained in the interval 375-425°; in this case the "nominal" contact time for achieving maximum yields substantially decreases as the temperature rises (Fig. 1). The yield of divinyl increases with increase of the contact time, up to a certain limit, after which the yield begins to decrease, obviously owing to secondary reactions. Besides divinyl, the contact gas contains some propylene, obviously obtained through the cracking of (I). Under optimum conditions, the propylene content is 6-7.5 % of the divinyl. The ratio of propylene to divinyl varies little with the degree of conversion (Fig. 1). At very high degrees of conversion only, this ratio increases, apparently owing to secondary reactions of cracking of the divinyl. This fact indicates that propylene is formed independently of the main reaction of divinyl formation and parallel to it. Allylcarbinol (IV) is always found in the reaction products. The yield curves (Figs. 2 and 3) pass through a maximum ("kinetic hump") which is characteristic of consecutive reactions, since allylcarbinol apparently is subsequently dehydrated to divinyl (see the reaction mechanism).

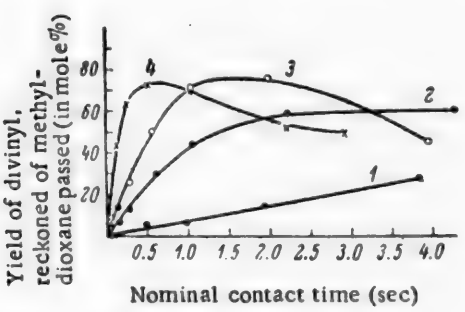


Fig. 1. Yield of divinyl on KSD catalyst at various temperatures and contact times. 1) 275°; 2) 325°; 3) 375°; 4) 425°.

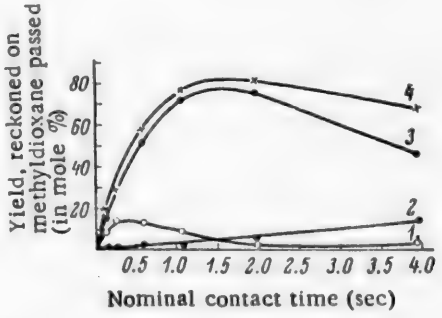


Fig. 2. Contact conversion of 4-methyldioxane on KSD catalyst at 375° and 1 : 20 (molar) dilution by water vapor. 1) Allylcarbinol; 2) charcoal; 3) divinyl; 4) unsaturated hydrocarbons ($C_4H_6 + C_5H_6$).

When the contact process is carried out under milder conditions (at lower temperatures and shorter contact time) so that a relatively slight degree of conversion of methyldioxane (I) (50-60%) is obtained, the amount of allylcarbinol (IV) may be considerably increased. Thus, at 350° and 0.4 sec contact time the degree of conversion of (I) per pass is 60%, and the molar yields of divinyl and (IV), reckoned on passed and decomposed (I), are about equal (Fig. 3). Increase of the contact time under these conditions also leads to a sharp decrease in the yield of (IV).

TABLE 1

Effect of Dilution of Water Vapor on the Contact Cleavage of 4-Methyldioxane-1,3 on KSD

Temp.	Space velocity (ml/ml of cat./hr)		Nominal contact time (sec)	Dilution of methyldioxane by water vapor (in moles)	Methyldioxane conversion to unsat. hydrocarbons (divinyl + propylene) (mole %)	Divinyl cont. in unsat. part of contact gas (vol. %)	Yield of divinyl, reckoned on methyldioxane passed (mole %)
	methyldioxane	water					
377°	0.24	0.25	2.73	6.1	66.7	79.2	52.8
375	0.22	0.39	1.82	10.5	68.5	80.8	55.4
376	0.22	0.96	0.78	25.1	72.6	86.2	62.6
376	0.22	1.41	0.55	37.1	78.6	92.5	72.6
370	0.24	1.84	0.42	44.4	82.0	91.5	75.1
372	0.24	2.42	0.32	58.5	73.1	91.0	66.4

Dilution of methyldioxane (I) by water vapor leads to substantial acceleration of the reaction. As is evident from the data of Table 1, an increase in the proportion of water from 6 to 44 moles per mole of (I) with the corresponding decrease in the contact time not only did not decrease, but even somewhat increased the degree of conversion of (I). On the basis of this fact it was concluded that water participates directly in the reaction.

Experiments in continuous contact showed that the degree of conversion of (I) and the yields of divinyl diminish every hour. Hence, the time of operation of the catalyst before regeneration must not exceed 4 hours. When the operating time of the catalyst before regeneration is 8 hours, the yield of divinyl, reckoned on passed (I), is 25% lower than when the time is 2 hours. The stability of the catalyst proved to be very satisfactory. After 700 hours of operation the catalyst was still as active as at the beginning of the test. In experiments of 2-hours' duration (before regeneration) the average yield of divinyl for the last 400 hours was 77%, reckoned on passed (I), or 84%, reckoned on decomposed (I).

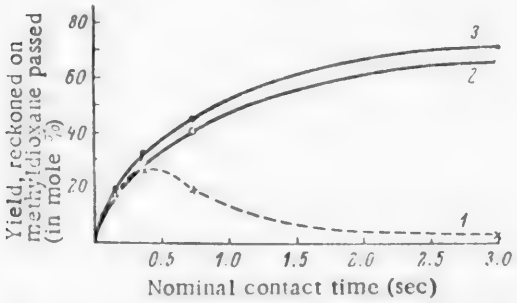


Fig. 3. Contact conversion of 4-methyldioxane on KSD catalyst at 350° and 1 :12 (molar) dilution by water vapor. 1) Allylcarbinol; 2) divinyl; 3) unsaturated hydrocarbons.

Study of the Conversions of Allylcarbinol. Allylcarbinol (IV), as we have seen, is one of the products of the catalytic cleavage of methyldioxane (I). Along with undecomposed (I), it is distilled from the "furnace" condensate in the form of close-boiling azeotropes with water. Allylcarbinol may be used both for divinyl preparation and other syntheses. In the latter case, it is expedient to carry out the contact cleavage of (I) under conditions providing the maximum yield of allylcarbinol along with divinyl (see above). (IV) is smoothly dehydrated to divinyl on KSD catalyst under the conditions chosen for contact conversion of the principal product (I). The experimental results given in Table 2 show that even at 350° (IV) is dehydrated smoothly with a good yield of divinyl. At 375° the conversion of (IV) is practically quantitative.

TABLE 2

Dehydration of Allylcarbinol on KSD Catalyst

Temperature	Space velocity (ml/ml of catalyst per hour)		Total conversion of allylcarbinol (in %)	Yield, reckoned on allylcarbinol passed (mole %)		
	allylcarbinol	water		divinyl	propylene	carbon
350°	0.230	0.694	88.7	73.2	10.8	1.4
375°	0.237	0.737	98.0	82.0	9.7	2.1

A very expedient technical use of (IV) lies in its conversion to butanol-1 (V) by hydrogenation; our experiments show that this can be carried out with quantitative yields [6]. Butanol-1 is an important product of primary organic synthesis; at present there are only a few methods for its preparation. Allylcarbinol (IV) may be another starting material for syntheses of hitherto unavailable derivatives of tetrahydropyran. It was shown that (IV) smoothly reacts with formaldehyde in the presence of acid to form 4-hydroxytetrahydropyran (III) in near-quantitative yields [4]. For a number of syntheses (IV) must be isolated from the catalyzate in a pure state. In our case, this is complicated by the proximity of the boiling points of (IV) and undecomposed (I), both in the pure state and in the form of their azeotropes with water. A method for separating (I) and (IV) from the catalyzate by azeotropic distillation in the presence of toluene was developed [8]; (I) does not form an azeotrope with toluene, whereas (IV) gives an azeotrope with b. p. 103.6° in which the content of (IV) is 33.6%.

In order to evaluate the results more carefully, a number of material-balance experiments were performed, in which all reaction products were taken into account as far as possible. In Table 3 are given typical material balances for "divinyl" conditions, and also "allylcarbinol" conditions (i.e., conditions providing simultaneous formation of the maximum amount of allylcarbinol together with divinyl).

The aqueous condensate, formed in the contact cleavage of methyldioxane (I), contains unreacted (I), allylcarbinol (IV), and formaldehyde. The yields of formaldehyde formed as a result of the reaction [one mole of formaldehyde per mole of divinyl and per mole of (IV), and two moles per mole of propylene] varied from 89 to 93% in the material-balance experiments; (I) and (IV) may be distilled from the condensate in the form of azeotropes. After distillation of the aqueous azeotropes of (I) and (IV) the condensate consists of a dilute

(5-7%) formaldehyde solution. The latter may be returned to the process (for condensation with propylene) in the form of a standard 37% solution by concentration under pressure [9].

Contact Conversion of 4-Hydroxytetrahydropyran. The main by-product in the reaction of propylene with formaldehyde is 4-hydroxytetrahydropyran (III), the amount of which is 7-10%, reckoned on reacted formaldehyde. It may be of interest in itself and may find use in the synthesis of a number of substances (e.g., derivatives of tetrahydropyran [4], esters, etc.). It was of interest to us, however, to study the direction of contact conversion of (III) on KSD catalyst.

TABLE 3

Material-Balance Experiments in the Contact Conversion of 4-Methyldioxane-1,3 on KSD Catalyst Reaction Conditions: A) "divinyl regime," temperature 375°, space velocity 0.22 ml/ml of catalyst per hour, dilution by water vapor 1 : 18 (molar); amount of methyldioxane (I) passed, 70.3 g (0.6892 mole); B) "allylcarbinol regime," temperature 350°, space velocity 0.55 ml/ml of catalyst per hour, dilution by water vapor 1 : 12 (molar); methyldioxane (I) passed, 107.8 g (1.058 mole).

Reaction products obtained	A			B		
	Weight (in g)	yield, reckoned on methyldioxane (in mole %)		Weight (in g)	yield, reckoned on methyldioxane (in mole %)	
		passed	decomposed		passed	decomposed
Divinyl	26.14	70.30	82.00	16.0	28.0	46.0
Propylene	1.78	5.92	6.85	1.4	3.1	5.1
Allylcarbinol	4.24	8.55	–	17.6	23.1	38.0
Recovered methyldioxane	3.96	5.65	–	42.2	39.2	–
Low-boiling liquid* products (60-80° fraction; contains 25% butyraldehyde)	1.72	3.48	4.05		–	–
Carbon on the catalyst	1.1	2.35	2.75	0.4	0.6	1.1
Losses	–	3.75	4.35	–	6.0	9.8
Total		100	100		100	100

* On calculating yields in experiments performed under the conditions for divinyl preparation, the low-boiling liquid products were arbitrarily taken to be butyraldehyde, and allylcarbinol was considered equivalent to recovered methyldioxane.

When (III) is passed over this catalyst under the usual conditions for contact cleavage of (I) [temperature 375°, space velocity of (III), 0.6, and dilution by water vapor, 1 : 2 by weight], the (III) is dehydrated to a considerable extent, 2,3-dihydro- α-pyran (VIII) being formed [36 mole %, reckoned on passed (III)]. Products formed besides (VIII) include 15-20% of divinyl and about 5% of the unsaturated alcohol [mainly (IV)], both reckoned on passed (III). In the condensate 95-98% of formaldehyde is found.

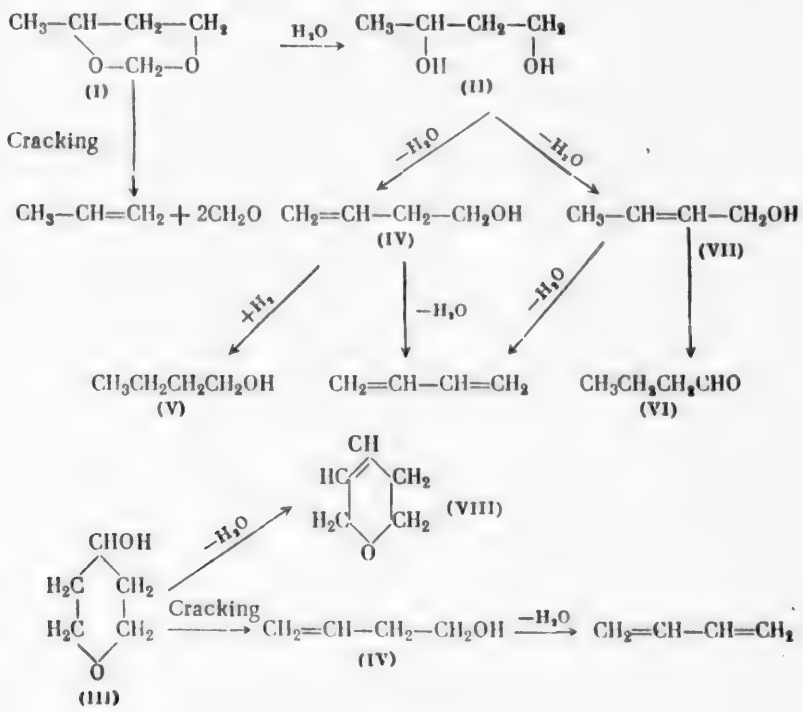
The yield of divinyl substantially increases when the reaction is carried out under more severe conditions. Thus, if (III) is passed over the catalyst at 500 and 550° (space velocity, 0.4, dilution by water vapor, 1 : 2 by weight), the yield of divinyl, reckoned on passed (III), increases to 50.3 and 69.5 mole %, respectively.

Reaction Mechanism. Earlier we showed (Table 1) that the contact cleavage of methyldioxane (I) is substantially accelerated as the water-vapor concentration increases. This fact indicates that water definitely takes part in the reaction. In our opinion, the first stage of the reaction is the hydrolysis of (I) to butanediol-1,3 (II) in the presence of water vapor, formaldehyde being split out. The butanediol, adsorbed on the catalyst, is dehydrated at a rate more rapid than that of its possible desorption and evolution into the gas phase. In this case,

dehydration of (II) takes place with splitting-out of one or two molecules of water and the corresponding conversion to allylcarbinol (IV) and divinyl. The formation of (IV) and that of divinyl are consecutive reactions, as is indicated by the characteristic maximum in the kinetic curves of dependence of the yield of (IV) on the contact time (Figs. 1 and 3). The character of the catalyst, which has hydrolyzing and dehydrating properties simultaneously, also favors the reaction in this direction. Thus, with this catalyst under conditions similar to those described, methylal was smoothly hydrolyzed to methanol [10]; the smooth dehydration of (IV) to divinyl also is described in the cited article.

Besides the main reaction, cracking of (I) to propylene and formaldehyde takes place as a side reaction which goes at a low rate under the chosen conditions. The formation of butyraldehyde (VI), which we found in the low-boiling fraction (60-80°) of the condensate, may be explained by isomerization of the β-unsaturated crotyl alcohol (VII), which we found in small amounts along with allylcarbinol (IV).

4-Hydroxytetrahydropyran (III) is dehydrated under mild conditions with the formation of (VIII). The mechanism of formation of divinyl from (III) is apparently one of selective cracking, in which a molecule of (III) is decomposed, formaldehyde and a C_4-alcohol fragment being split out. The latter either changes to (IV), which is more stable under the reaction conditions, or is further dehydrated, divinyl being formed. The stated conversions are shown in Scheme 2.



Scheme 2

EXPERIMENTAL*

The laboratory setup in which the work was done, the method of its use, and the evaluation of the experimental results were described earlier by us [7]. The method of preparing KSD catalyst and the contact-process parameters used were described in the same work.

* N. K. Shemyakina assisted in the experimental part.

4-Methyldioxane (I) (technical) was redistilled in a laboratory column with 17 theoretical plates, and had the constants: b. p. 114-116° $n^{20}D$ 1.4165, d^{20}_4 0.9741.

Literature data [3]: b. p. 115.3°, $n^{20}D$ 1.4159, d^{20}_4 0.9758; azeotrope of (I) with water: b. p. 88.3°; content of (I) 76.75%, H_2O 23.25% [3, 6].

Allylcarbinol (IV) – technical, with a (IV) content of 95.15% (determined by the bromide-bromate method), $n^{20}D$ 1.4219, d^{20}_4 0.8478; azeotrope of (IV) with water: b. p. 92.7°; content of (IV) 59.6%, H_2O 40.4% [3, 6].

4-Hydroxytetrahydropyran (III) – technical, b. p. 85-95° (at 20 mm), $n^{20}D$ 1.4585, d^{20}_4 1.0701.

Literature data [3]: b. p. 190°, $n^{20}D$ 1.4600, d^{20}_4 1.0708.

Method of Analyses. The divinyl content in the gas, collected on contact and blowing-out of the condensate, was determined by bromination [11].

Allylcarbinol (IV) and undecomposed methyldioxane (I) were determined in the fraction distilled from the condensate up to 96°, containing aqueous azeotropes of (I) and (IV). In this case, the (IV) content was determined by the bromide-bromate method [11]; in certain cases this determination was checked by the phthalization method [12]. (I) was determined by the method of hydrolysis in the presence of hydroxylamine salts [10]. The formaldehyde content in the condensate was determined by the iodine method according to Romiin. The content of unsaturates in the gas was determined through absorption by 84% H_2SO_4 in an Orsat apparatus; the difference between the content of unsaturated hydrocarbons in the gas and the divinyl content was ascribed to propylene.

Material-Balance Experiments. On carrying out the material-balance experiments the contact conversion products from a number of experiments, performed under identical conditions, were combined. Gas analysis was carried out as stated above. The condensate was distilled in a column with an efficiency of 45 theoretical plates. Owing to the fact that the individual fractions were stratified liquids, the distillate was taken off in the vapor phase. The main clearly separated fractions were the azeotrope of methyldioxane (I) with water (b. p. 88°) and the azeotrope of allylcarbinol (IV) with water (b. p. 92°); the content of (I) and (IV) in these fractions was also determined analytically. Butyraldehyde was found in the low-boiling fraction (60-80°) and was also determined analytically. The amount of "carbon" on the catalyst was determined from the amount of carbon dioxide in the contact gas and the regeneration gases [7].

Divinyl. The maleic anhydride adduct, m. p. 102.5-103.5°, was prepared for identification. Part of the tetrahydrophthalic anhydride obtained was boiled with water until completely dissolved; crystals with m. p. 164.5-165° (tetrahydrophthalic acid) separated out on cooling.

Allylcarbinol (IV) was isolated from its azeotrope with water by salting out and then drying with potash and distilling in a precision column.

B. p. 114.2-115°; d^{20}_4 0.8453, $n^{20}D$ 1.4212. Acetate: b. p. 124.7-125.2°, d^{20}_4 0.9302, $n^{20}D$ 1.4206. 3,5-Dinitrobenzoate: b. p. 152° (from alcohol).

Literature data: b. p. 112-113.5° (755 mm), $d^{17.5}_4$ 0.8379, $n^{17.5}D$ 1.4146. Acetate: b. p. 125°, d^{20}_4 0.934.

Hydrogenation of Allylcarbinol (IV). The azeotrope of allylcarbinol with water (separated by azeotropic distillation with toluene), containing 57.4% (IV), 0.14% methyldioxane, and 48.46% water, was used for the reaction. The hydrogenation was carried out over "copper-chromite" catalyst, reduced, according to directions in [13], in an oscillating autoclave. The autoclave was charged with 6 g of catalyst, 60 ml of methanol, 154 g of the azeotrope [1.33 moles of (IV)], and hydrogen to 80 atm pressure at 18°. The hydrogenation was carried out, with heating, for 1.5 hours. At the end of the reaction the temperature was 140°. The amount of hydrogen consumed was 22.2 liters (1.26 moles). The hydrogenation products were filtered to remove the catalyst, the latter washed with methanol, and the filtrate and washings fractionally distilled. The yield of butanol-1 was quantitative.

B. p. 117-117.5°, d^{20}_4 0.8095, $n^{20}D$ 1.3999. Literature data: b. p. 117.4°, d^{20}_4 0.80978, $n^{20}D$ 1.39991.

Butyraldehyde (VI) was determined from the low-boiling fraction (60-80°), in the form of the 2,4-dinitrophenylhydrazone, m. p. 123-124°. A mixed sample with a known preparation gave no melting-point depression.

Contact Conversion of 4-Hydroxytetrahydropyran (III). A total of 102 g of (III) was passed under the conditions stated above, and 330 g of condensate was obtained, which was distilled in a column with 70 theoretical plates, the distillate being taken off in the vapor phase. The upper layer of the fraction with b. p. 76-76.5° was dried with potash and redistilled. Twenty g of 2,3-dihydro-α-pyran (VIII) was obtained.

B. p. 93°, d^{20}_4 0.9389, $n^{20}D$ 1.4480, MR_D 23.97; Calc. 24.26. Bromine number 188; calc. 190.

Literature data [4]: b. p. 93°, d^{20}_4 0.9394, $n^{20}D$ 1.4480.

SUMMARY

1. The synthesis of divinyl, based on the interaction of propylene and formaldehyde, was studied, and a catalyst for this process was chosen.

2. A yield of divinyl equal to 70%, reckoned on methyldioxane passed, or 82%, reckoned on that decomposed, was attained as a result of studying the conditions of contact cleavage of methyldioxane (the main product of the reaction of propylene with formaldehyde).

3. The possibility of simultaneous synthesis of divinyl and allylcarbinol (in approximately equal proportions by weight) in 84% yield reckoned on decomposed methyldioxane was shown. In this case, the expediency of using allylcarbinol for the synthesis of butanol-1 by quantitative hydrogenation of the former is noted.

4. The contact conversion of 4-hydroxytetrahydropyran (a by-product of the reaction of propylene with formaldehyde) was studied. A reaction mechanism for the formation of the contact-conversion products, methyldioxane and 4-hydroxytetrahydropyran, is proposed.

LITERATURE CITED

1. M. I. Farberov, et al., New Method of Synthesis of Dienes of the Divinyl Series [in Russian] (Izd. MkhP, 1952).
2. M. I. Farberov, Doklady Akad. Nauk SSSR 110, 1005 (1956).*
3. M. I. Farberov, Ya. I. Rotshtein, A. M. Kut'in, and N. K. Shemyakina, Zhur. Obshch. Khim. 27, 2806 (1957).*
4. M. I. Farberov, E. P. Tepenitsyna, and N. K. Shemyakina, Doklady Akad. Nauk SSSR 99, 793 (1954); Zhur. Obshch. Khim. 25, 133 (1955).*
5. E. Arundale and L. Mikeska, Chem. Revs. 51, 505 (1952); Uspekhi Khim. 23, 223 (1954).
6. M. I. Farberov, A. M. Kut'in, T. P. Vernova, and N. K. Shemyakina, Nauch. Doklady Vuzov 1, 148 (1958).
7. M. I. Farberov, A. M. Kut'in, G. I. Kishinskii, and T. P. Vernova, Zhur. Obshch. Khim. 30, 875 (1960).*
8. A. F. Frolov and G. V. Novikova, Uchenye Zapiski YarTI 2, 113 (1957).
9. M. I. Farberov and V. A. Speranskaya, Zhur. Priklad. Khim. 28, 222 (1955).*
10. M. I. Farberov and N. K. Shemyakina, Zhur. Obshch. Khim. 26, 2749 (1956).*
11. Analysis of the Products of Synthetic Alcohol and Synthetic Rubber Production [in Russian] (GKhI, 1957).
12. P. Elving and J. Warshowsky, Anal. Chem. 19, 1006 (1947).
13. H. Adkins, E. E. Burgoyne, and H. I. Schneider, J. Am. Chem. Soc. 72, 2626 (1950).

* Original Russian pagination. See C. B. translation.

REACTION OF tert-BUTYL LITHIUM WITH ESTERS

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It has been shown in a number of investigations [1] that tert-butylmagnesium halides react with esters by anomalous routes that lead to symmetrical ketones with radicals corresponding to those of the acids used, to secondary alcohols that are reduction products of these ketones, to disecondary alcohols, etc. The mechanism of this reaction, which takes place in the case of the esters of low molecular weight acids at ordinary temperatures (in ether), but in the case of the esters of high molecular weight acids at elevated temperatures up to 100° (in xylene), has been represented by the schemes shown below.

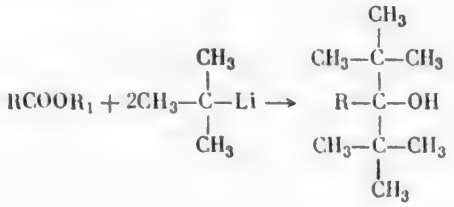
$$2RCOOR_1 + 2R_2MgX \rightarrow 2RCOOMgX + (R_2 + H) + (R_2 - H) + (R_1 + H) + (R_1 - H) \rightarrow RCOR + MgCO_3 + MgX_2 \quad (1)$$

or

$$2R_2MgX \rightarrow Mg(R_2)_2 + MgX_2;\ 2RCOOR_1 + 2MgX_2 \rightarrow 2R_1X + 2RCOOMgX \text{ etc.} \quad (2)$$

The possibility of saponification of the ester under these conditions was experimentally verified by heating heptyl palmitate with anhydrous magnesium chloride, as a result of which heptyl chloride was isolated [2]. It was also established [3] that when Mg was replaced by Na and when a mixture of tert-butyl chloride and the esters of butyric or isobutyric acid were added to the latter, only in the case of the latter ester was it possible to carry out the reaction according to the normal scheme and obtain di-tert-butylisopropylcarbinol in small yield (19%). In the case of the butyric acid ester, however, tert-butyl propyl ketone and the secondary alcohol corresponding to it were obtained.

In the present investigation we substituted Li for the Na and changed from a one-stage to a two-stage scheme for carrying out the synthesis, whereby the condensation of the Li alkyl with the esters was accomplished at a very low temperature (− 35 − 40°). Under these conditions, which guaranteed that the reaction would go predominantly by the route of a pure organometallic synthesis



(3)

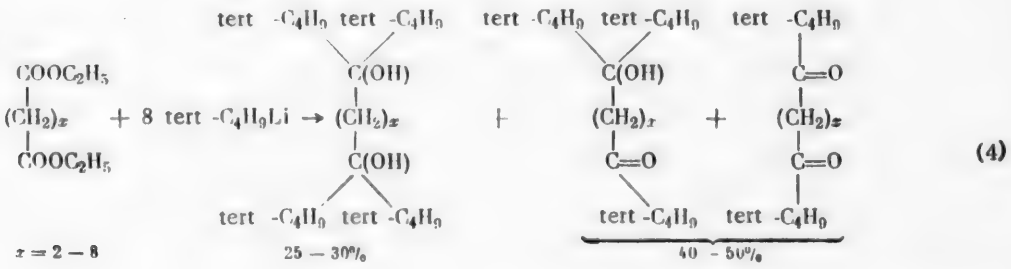
we obtained very high yields of the tertiary alcohols, varying within the range 85-60% for the first members of the series of esters (in the case of a 2-fold excess of tert-butyl lithium over the theoretical). The yield of the

alcohols decreased with an increase in the length of R; for the ester of enanthic acid it fell to 50% and for the ester of undecylenic acid to 30%. A characteristic peculiarity of this reaction was the complete absence of side reduction processes in the synthesis of the alcohols – even in the case of the reaction with the ester of formic acid. We should keep in mind that, as Favorskii and Kolotova showed [4], tert-C_4H_9MgCl reacts with this ester according to the scheme

$$HCOOC_2H_5 + 2\ \text{tert-}C_4H_9MgCl \rightarrow \text{tert-}C_4H_9CH_2OH + MgClOH + \\ + MgCl(OC_2H_5) + CH_2{=}C(CH_3)_2.$$

Ketones of the type RCOR were found in this reaction in traces only in the case of such a high molecular weight ester as that of undecylenic acid.

In view of the great effect on the alcohol yield of an excess of the lithium alkyl established in the example of the esters of monobasic acids, all the experiments with the esters of dibasic acids were carried out with a 2-fold excess of lithium alkyl as compared with the theoretical (i.e., with a 1:8 ratio of ester to lithium alkyl). However, the yields of ditertiary glycols from the esters of such acids as adipic, azelaic, and sebacic varied within the limits 25-30%, i.e., they were $^1/_2$ to $^1/_3$ of the yields of tertiary alcohols under similar conditions. Along with the ditertiary glycols, intermediate products of the synthesis, diketones and keto alcohols (tertiary), were obtained in 40-50% yields. With a still larger excess of the lithium alkyl (1:16) we were able to raise the yield of the glycol to 52% in the case of the ester of adipic acid in one of the experiments. Thus, the reaction can be schematically represented for the above-mentioned esters of dibasic acids by the following equation



(4)

In an experiment with the ester of succinic acid, for which the steric hindrance is somewhat higher than in the case of the esters of higher molecular weight acids, the crystalline diketone tert-$C_4H_9-CO-(CH_2)_2-CO-C_4H_9$-tert was the predominant product. The intermediate product of the reaction, the keto alcohol, was obtained in low yield, and the glycol was not formed at all. In the case of the ester of oxalic acid, where the steric hindrances are still more appreciable, the ditertiary glycols again were not formed. The yield of the tertiary alcohol-ketone

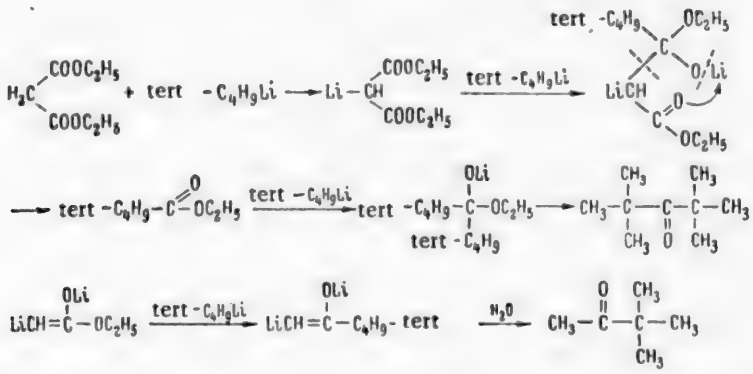
$$\text{tert-}C_4H_9{-}C(OH){-}CO{-}C_4H_9\text{-tert}$$
$$\text{tert-}C_4H_9$$

was very low and the main product of the reaction proved to be not the expected diketone (as in the case of the ester of succinic acid), but the corresponding keto alcohol (secondary).

It is known [5] that the ester of oxalic acid forms with tert-C_4H_9MgCl only the product of the first stage of the reaction, tert-$C_4H_9COCOOC_2H_5$ and the disecondary glycol tert-$C_4H_9CHOHCHOHC_4H_9$-tert, which indicates the large extent of the reducing reactions in the latter case.

The ester of malonic acid reacts with normal Mg halogen alkyls by the normal route. Thus [6] as a result of the reaction of the malonic ester with n-$C_{10}H_{21}MgBr$ 1,1,3,3-tetra-n-decylpropandiol-1,3 was obtained [6]. The malonic ester does not react with branched alkyl halides at all because of the development of greater steric hindrances and enolization. When malonic ester reacted with iso-C_3H_7MgCl, unreacted malonic ester and propane were obtained [7]. The reaction of malonic ester with tert-C_4H_9MgCl had not yet been studied by anyone.

We carried out this reaction in the present investigation and obtained back malonic ester plus a mixture of isobutane and isobutylene (in 3:2 ratio). The reaction with tert-butyl lithium went differently, and as a result we obtained pinacolin and hexamethylacetone. The following reaction scheme is suggested as probable.



Di-tert-butylcarbinol is produced, obviously, as a result of the reduction of hexamethylacetone.

EXPERIMENTAL

Preparation of tert-butyl lithium. There are two methods of preparing tert-butyl lithium. Gilman [8] prepared it in 50-65% yield by heating tert-butyl chloride with metallic lithium in petroleum ether for 8 hours. Bartlett [9] showed that tert-butyl lithium is easily prepared in 75% yield in diethyl ether at (– 35)-(–40°)by reacting tert-butyl chloride with lithium for 2-3 hours. We chose Bartlett's method. The syntheses were carried out in a two-liter flask fitted with an oil seal, a reflux condenser with a calcium chloride tube, a dropping funnel, and a stirrer. To prepare the organolithium compound from 41.7 g of lithium and 278 g of tert-butyl chloride, we placed in the flask 1 liter of absolute ether. The metallic lithium was cut into small pieces with shears in a current of nitrogen over a conical funnel and introduced through the latter into the reaction flask. The lithium prepared in this way (pieces 1 mm × 1 mm) retained its metallic luster and was completely suitable for the synthesis.

The reaction flask was placed in a bath with a cooling mixture (dry ice and acetone), after which the stirrer was turned on. When the temperature had dropped to – 35°, we began to add the tert-butyl chloride (b. p. 50.5-52.5°) dissolved in an equal volume of absolute ether, while maintaining the temperature of the reaction mixture at (–35)-(–40°). The reaction usually started at once and went smoothly to its termination in 3.5 hours. After all the chloride had been introduced, stirring was continued for 0.5 hour longer. During the addition of the chloride it was necessary to maintain strictly the required temperature. Cooling to – 50° could extinguish the reaction. At – 20° the appearance of a yellowish precipitate was observed and also a heating up of the reaction mixture, which was caused by the decomposition of the tert-butyl lithium by the ethyl ether [10]. When the chloride was added more rapidly to the lithium or at a higher temperature, we also often observed the evolution of a small amount of isobutylene, which probably was produced as a result of the decomposition of the lithium alkyl to olefin and lithium hydride [11].

Preparation of alcohols and glycols. A mixture of the ester and an equal volume of absolute alcohol was added to the organolithium compound that had been prepared. In the case of syntheses with esters of dibasic acids, the latter were diluted with 4 times their volume of ether to avoid their solidifying in the process of adding them at low temperature. The amount of ester used in the synthesis of the alcohols was $^1/_2$ or $^1/_4$ of the amount required according to Eq. (3). The reaction was carried out also at (–35)-(–40°) in an atmosphere of nitrogen and proceeded without the evolution of gases (except for syntheses with malonic ester). At – 55° and below, where the reaction goes slowly, it was mainly the intermediate condensation product, the ketone, that was obtained. After all of the ester had been added, the reaction mixture was stirred for 1.5 hours longer. The unreacted lithium was separated out by filtration and the reaction product was decomposed with ice and dilute hydrochloric acid and treated in the usual way. To remove the unreacted ester, the reaction products were

saponified with 15% alcoholic solution of NaOH for 6-18 hours. The unreacted lithium was decomposed with methyl alcohol and with water and was neutralized by titration with a solution of acid. On the average, about 4-10% of the lithium employed in the synthesis did not react.

1. Reaction of tert-butyl lithium with esters of aliphatic monobasic acids. The reaction of tert-C_4H_9Li with the methyl esters of the following acids was investigated: formic, acetic, propionic, butyric, isobutyric, valeric, isovaleric, caproic, enanthic, and undecylenic. The molar ratio of tert-butyl lithium and ester in the experiments was 4:1. The yield of condensation products – tertiary alcohols and ketones – and their properties are shown in Tables 1-3.

TABLE 1

Yield of Tertiary Alcohols and Ketones from the Reaction of $RCOOCH_3$ with tert-C_4H_9Li (in %)

R	H	CH_3	C_2H_5	iso-C_3H_7	n-C_3H_7	n-C_4H_9	iso-C_4H_9	n-C_5H_{11}	n-C_6H_{13}	n-$C_{10}H_{19}$
$RCOH(C_4H_9)_2$-tert	85.3 *	80.3	78.8	88.1	66.7	64.2	65.9	60.3	50.5	30.3
$R-\overset{\overset{O}{\parallel}}{C}-C_4H_9$-tert	–	6.5	6.9	1.1	11.3	14.5	15.6	22.5	30.6	24.6**

* Yield of secondary alcohol is shown.

** 1.3% of the ketone RCOR was obtained at the same time.

II. Reaction of tert-butyl lithium with esters of aliphatic dibasic acids. In view of the anomalous behavior of the first two representatives of the series of dibasic acids in this reaction, the experiments that were carried out with diethyl oxalate and with malonic ester are described in more detail and the data on the reaction of tert-C_4H_9Li with the dimethyl esters of succinic, adipic, azelaic, and sebacic acids are given in the tables. In all the experiments with dibasic acids the ratio of tert-butyl lithium to the ester was 8:1.

1) Reaction of tert-butyl lithium with diethyl oxalate. Used: 42 g of lithium, 278 g of tert-C_4H_9Cl, and 49 g of diethyl oxalate. When the reaction product was distilled from a Favorskii flask at 80-90° (4 mm), a crystalline product with a strong camphor odor distilled at 60°. Its properties were: m. p. 80-81° (from n-hexane), b. p. 201-204° (760 mm). The product was not changed by the action of concentrated H_2SO_4 at (–10)-(–20°) nor by prolonged storage (4 months) over P_2O_5. We were not able to determine the presence of a ketone group by making an oxime by heating. In the IR spectrum of this compound (solution in CCl_4) an absorption band was found at 1704 cm^{-1}, corresponding to the valence vibration of the C=O group.

Found %: C 69.81, 69.65; H 11.68, 11.56; OH 10.7, 11.2. M 177, 183 (in benzene). $C_{10}H_{20}O_2$. Calculated %: C 69.70; H 11.70; OH 9.87. M 172.3.

From the analytical data, we consider that the crystalline product was the secondary keto alcohol, the normal intermediate condensation product. The yield of the secondary keto alcohol was 37 g (57.3%). For evidence of the structure the product was oxidized with iodic acid by the method of Clutterbuck and Reuter [17]. We used for the oxidation 3 g of the keto alcohol and an equimolar quantity of aqueous-alcoholic solution of KIO_4 acidified with H_2SO_4. In the neutral oxidation products we identified trimethylacetaldehyde with a 2,4-dinitrophenylhydrazone of m. p. 204-205° (from alcohol).

Found %: N 20.79. $C_{11}H_{12}O_4N_4$. Calculated %: N 21.05.

In the acid oxidation products the presence of trimethylacetic acid was established. The latter was identified through the amide, which had an m. p. of 150° (from benzene). A mixed sample of the amide prepared by us and the pure amide of trimethylacetic acid melted at 151.5°.

TABLE 2

Properties of Alcohols of the Formula R—COH(tert-C_4H_9)$_2$

Expt. No	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Found (%) OH	Empirical formula	Calc. (%) C	Calc. (%) H	Calc. (%) OH	Literature data
1	H	116 * (164)	—	—	—	—	75.15, 75.14	14.04, 13.92	11.20	$C_9H_{20}O$	74.93	13.97	11.80	B.p. 117-118° (166 mm); m.p. 50° [12]
2	CH_3	104—106 ** (57)	—	—	—	—	76.13, 76.07	13.95, 13.95	11.20	$C_{10}H_{22}O$	75.88	14.01	10.80	B.p. 105° (57 mm), m.p. 37° [13]
3	C_2H_5	121—121.5 (55)	1.4517	0.8661	53.64	54.52	76.50, 76.61	13.89, 13.98	9.95	$C_{11}H_{24}O$	76.67	14.04	9.87	B.p. 117° (22 mm), n_D^{20} 1.4563, d_4^{20} 0.8593 [3]
4	n-C_3H_7	101 (22)	1.4542	0.8652	58.28	59.14	77.40, 77.35	14.09, 14.15	8.65	$C_{12}H_{26}O$	77.35	14.07	9.12	
5	iso-C_3H_7	78.5—79 *** (4)	1.4655	0.8853	58.40	59.14	77.50, 77.40	14.00, 14.09	9.00	$C_{12}H_{26}O$	77.35	14.07	9.12	n_D^{20} 1.4655, 1.4623 [3]
6	n-C_4H_9	121.5—123 (24)	1.4540	0.8596	63.05	63.76	78.14, 78.00	14.21, 14.20	8.80	$C_{13}H_{28}O$	77.93	14.09	8.49	—
7	iso-C_4H_9	133—134 (40)	1.4573	0.8676	62.54	63.76	78.05, 78.03	14.19, 14.08	8.70	$C_{13}H_{28}O$	77.93	14.09	8.49	—
8	n-C_5H_{11}	137—138 (22)	1.4553	0.8614	67.55	68.38	78.68, 78.65	14.32, 14.25	8.20	$C_{14}H_{30}O$	78.43	14.11	7.93	—
9	n-C_6H_{13}	128 (7.5)	1.4569	0.8603	72.18	72.99	78.35, 78.52	14.03, 13.95	6.91	$C_{15}H_{32}O$	78.85	14.14	7.45	—
10	n-$C_{10}H_{19}$	162—163 (4)	1.4674	0.8698	91.00	90.20	80.93, 80.85	13.62, 13.66	5.77	$C_{19}H_{38}O$	80.78	13.56	6.03	—

* M. p. 51-52°.

** M. p. 37-38°.

*** The alcohol crystallized 7 days after its preparation, m. p. 24°.

TABLE 3

Properties of Ketones of the Formula R—CO—tert-C_4H_9

Expt. No.	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Empirical formula	Calc. (%) C	Calc. (%) H	Melting point of derivative	%N found	%N calc.	Literature data
1	CH_3	103—106° (749)	1.3995	0.8057	30.10	29.92	—	—	$C_6H_{12}O$	—	—	2,4-Dinitrophenylhydrazone 125-125.5°	20.03, 20.13	20.00	B.p. 103-106° (746 mm) [14]
2	C_2H_5	124—126 (758)	1.4109	0.8119	35.23	34.54	—	—	$C_7H_{14}O$	—	—	Semicarbazone 144-145°	—	—	B.p. 125-126° (769 mm), d_4^{20} 0.8125; semicarbazone m.p. 144° [15]
3	n-C_3H_7	42—44 (22)	1.4113	0.8145	39.10	39.16	74.86, 74.95	12.49, 12.51	$C_8H_{16}O$	74.94	12.58	Oxime 75-76°	10.00, 9.90	9.79	n_D^{20} 1.4115, d_4^{20} 0.8105, oxime m.p. 76-77° [3]
4	iso-C_3H_7	130—135 (760)	1.4060	0.8051	39.04	39.16	74.82, 74.79	12.47, 12.43	$C_8H_{16}O$	74.94	12.58	Oxime 139-140°	9.70, 9.61	9.79	n_D^{20} 1.4059, d_4^{20} 0.8054, oxime m.p. 141° [3]
5	n-C_4H_9	69.5—70 (24)	1.4162	0.8168	43.76	43.77	75.78, 75.88	12.74, 12.83	$C_9H_{18}O$	76.00	12.76	2,4-Dinitrophenylhydrazone 117-118°	17.34, 17.14	17.60	B.p. 164° (735 mm), d_4^{11} 0.823, semicarbazone m.p. 142-143° [16]
6	iso-C_4H_9	64.5—65 (42)	1.4190	0.8182	43.90	43.77	75.79, 75.88	12.68, 12.76	$C_9H_{18}O$	76.00	12.76	2,4-Dinitrophenylhydrazone 94-95°	17.29, 17.19	17.60	B.p. 157-158°, semicarbazone m.p. 145° [16]
7	n-C_5H_{11}	88—89 (22)	1.4212	0.8202	48.35	48.39	76.98, 77.05	12.25, 12.16	$C_{10}H_{20}O$	76.85	12.90	2,4-Dinitrophenylhydrazone 100-101°	16.63, 16.79	16.86	B.p. 72° (10 mm), d_4^0 semicarbazone m.p. 139-140° [16]
8	n-C_6H_{13}	87—89 (7.5)	1.4270	0.8237	52.98	53.01	78.10, 78.10	13.46, 13.51	$C_{11}H_{22}O$	77.58	13.02	2,4-Dinitrophenylhydrazone 62-63°	16.08, 16.14	16.00	
9	n-$C_{10}H_{19}$	128—129 (4)	1.4772	0.8543	70.70	71.01	80.08, 80.16	12.48, 12.54	$C_{15}H_{28}O$	80.29	12.58	2,4-Dinitrophenylhydrazone 50-51°	13.58, 13.69	13.77	

The fraction with b. p. 115-128° (4 mm), which was obtained in the amount of 4 g (4.7%), apparently was the impure keto alcohol.

Found %: C 73.54, 73.47; H 12.85, 12.69. $C_{14}H_{28}O_2$. Calculated %: C 73.63; H 12.36.

TABLE 4

Yield of Products of Condensation of Esters of Dibasic Acids $CH_3OOC(CH_2)_nCOOCH_3$ with tert-C_4H_9Li (in %)

n	2	4	7	8
Diketone				
CO-tert-C_4H_9 | $(CH_2)_n$ | CO-tert-C_4H_9	11.2	15.0	7.0	10.0
Ketoalcohol (tertiary)				
CO-tert-C_4H_9 | $(CH_2)_n$ | COH-(tert-C_4H_9)$_2$	3.8	30.2	39.1	—
Ditertiary glycol				
COH-(tert-C_4H_9)$_2$ | $(CH_2)_n$ | COH-(tert-C_4H_9)$_2$	—	26.3	36.2	31.0

2. Reaction of tert-butyl lithium with malonic ester. Used: 42 g of lithium, 278 g of tert-C_4H_9Cl, and 54.2 g of malonic ester. During the addition of the malonic ester to the organolithium compound a violent reaction took place and the evolution of gas was observed. Instead of the expected glycol and the intermediate condensation products, we obtained pinacolin, hexamethylacetone, and its reduction product, 2,2,4,4-tetramethylpentanol-3. The products from two replicate syntheses without saponification were distilled on a column. The following materials were separated.

a) Pinacolin – 33.1 g, b. p. 103-108° (755 mm), $n^{20}D$ 1.3985, d^{20}_4 0.8057, MR_D 30.15; calc. 29.92. Semicarbazone (from water) melted at 154-155°. 2,4-Dinitrophenylhydrazone (from alcohol) melted at 124.5-125.5°.

Found %: N 20.03, 20.13. $C_{12}H_{16}O_4N_4$. Calculated %: N 20.00.

Literature data [14]: b. p. 103-106° (746 mm).

2,4-Dinitrophenylhydrazone, m. p. 125°.

b) Hexamethylacetone – 51.4 g, b. p. 152-153.5° (755 mm), $n^{20}D$ 1.4203, d^{20}_4 0.8249, MR_D 43.69; calc. 43.97.

Literature data [18]: b. p. 152°, $n^{18}D$ 1.4195.

Seven grams of hexamethylacetone was reduced with metallic sodium in alcohol. We obtained 5.8 g of 2,2,4,4-tetramethylpentanol-3, m. p. 51-52°.

Found %: OH 11.5. $C_9H_{20}O$. Calculated %: OH 11.8.

TABLE 5

Properties of Products of Condensation of Esters of Dibasic Acids with tert-C_4H_9Li

Ditertiary Glycols of the General Formula $(tert\text{-}C_4H_9)_2COH-(CH_2)_n-COH(tert\text{-}C_4H_9)_2$

n	Boiling point (pressure in mm)	Melting point	Found (%)			Empirical formula	Calculated (%)			M	
			C	H	OH		C	H	OH	found	calculated
4	184—186° (2 mm)	104—105°	77.05, 77.15	13.40, 13.24	10.20	$C_{22}H_{46}O_2$	77.12	13.53	9.97	330	324.6
7	222—225 (1.5 mm)	54—55	78.15, 77.96	13.74, 13.70	8.92	$C_{25}H_{52}O_2$	78.05	13.63	8.83	—	—
8	229—234 (1 mm)	43—49	78.62, 78.53	13.89, 13.76	8.75	$C_{26}H_{54}O_2$	78.32	13.65	8.50	383	398.7

Diketones of the General Formula $tert\text{-}C_4H_9-CO-(CH_2)_n-CO-tert\text{-}C_4H_9$

n	Boiling point (pressure in mm)	Melting point	n_D^{20}	d_4^{20}	MR_D		Found (%)		Empirical formula	Calc. (%)		M		Melting point of 2,4-Dinitrophenylhydrazone	% N		
					found	calc.	C	H		C	H	found	calc.		found	calculated for monoderivative	calculated for diderivative
2	133—135° (8)	86—87°	—	—	—	—	72.55, 72.78	11.27, 11.31	$C_{12}H_{22}O_2$	72.68	11.18	192	198.3	185.5—186.5°	17.97, 17.92	14.80	20.06
4	143—145 (2)	49.5—50.5	—	—	—	—	74.47, 74.32	11.57, 11.53	$C_{14}H_{26}O_2$	74.28	11.58	229	226.4	236—237	15.38, 15.87	13.77	19.10
7	162—165 (1.5)	—	1.4562	0.9023	80.87	80.73	75.53, 75.69	12.22, 12.14	$C_{17}H_{32}O_2$	76.06	12.02	—	—	183—184	14.16, 14.58	12.48	17.83
8	178—182 (1)	—	1.4598	0.9049	85.26	85.34	76.56, 76.75	11.79, 11.85	$C_{18}H_{34}O_2$	76.54	12.13	—	—	150—152	17.35, 17.23	—	17.43

TABLE 5 (Continued)

Keto Alcohols (Tertiary) of the General Formula tert-$C_4H_9-CO-(CH_2)_n-COH$ (tert-C_4H_9)$_2$

n	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Found (%) OH	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) OH	Melting point of 2,4-Dinitrophenylhydrazone	%N found	%N calc.
2	152—155 (8)	1.4748	0.9250	77.46	77.62	75.14, 75.62	12.24, 12.35	5.60	$C_{16}H_{32}O_2$	74.94	12.58	6.60	82—83°	12.80, 12.62	12.85
4	159—162 (2)	1.4680—1.4690	0.9146—0.9148	87.40	87.96	76.57, 76.48	12.93, 12.89	5.50	$C_{18}H_{36}O_2$	76.00	12.76	5.97	114.5—115.5	11.84, 12.04	12.06
7	194—196 (1.5)	1.4694	0.9103	100.0	100.71	77.21, 77.13	13.12, 13.09	4.80	$C_{21}H_{42}O_2$	77.24	12.96	5.21	177	11.07, 11.24	11.06

c) 2,2,4,4-Tetramethylpentanol-3 – 6.2 g, b. p. 165-169° (755 mm). After recrystallization from n-hexane, m. p. 51-52°. A mixed sample gave no depression in melting point.

Literature data [12]: b. p. 117-118° (166 mm), m. p. 50°.

The alcohol was formed by the reduction of hexamethylacetone in the process of decomposition of the unreacted lithium that was present in the reaction mixture. In a supplementary experiment, it was shown that if the lithium was filtered off, the alcohol was absent from the products of the synthesis.

3. Reaction of tert-C_4H_9MgCl with malonic ester. Tert-C_4H_9MgCl was prepared from 73 g of powdered metallic magnesium and 278 g of tert-C_4H_9Cl. Addition of the chloride to the magnesium was extended over 7 hours with gentle boiling of the ether, after which the mixture was stirred for 1 hour more. During the addition of the malonic ester (54.2 g) at 35° over a period of 4 hours, the evolution of gas was observed. The gas was passed through a coil condenser that was placed in a cooling mixture with a temperature of – 80°. At the end of the experiment, the condensate was evaporated and passed over into a gas pipet. Analysis of the gas showed the presence of 44% of unsaturated and 56% of saturated hydrocarbons in it. After the addition of all the malonic ester, the reaction mixture (bright red in color) was stirred for 1 hour more. The reaction product was decomposed with an aqueous solution of ammonium chloride and was treated in the usual way. As a result of distillation we obtained 47 g of pure malonic ester. B. p. 196-201°, $n^{20}D$ 1.4142, d^{20}_4 1.0545.

In Tables 4 and 5 the results of the experiments on the condensation of tert-butyl lithium with the dimethyl esters of succinic, adipic, azelaic, and sebacic acids are given.

SUMMARY

1. It has been shown that in contrast to tert-butylmagnesium chloride, which reacts with esters by anomalous routes, tert-butyl lithium reacts at (– 35)-(– 40°) with the esters of both monobasic and dibasic acids by the normal mechanisms. In the case of the esters of a number of monobasic acids – saturated acids from C_2 to C_9 and unsaturated undecylenic acid – the yield of tertiary alcohols varied from 80 to 30%. Along with the alcohols, intermediate products were obtained – ketones of the type $RCOR_2$ – the yield of which increased with an increase in the length of the radical of the acid in the starting ester.

In the case of the ester of formic acid, the product of normal reaction, di-tert-butylcarbinol, also was obtained in 85% yield.

2. In the case of the esters of dibasic acids of high molecular weight (adipic, azelaic, sebacic) the yield of ditertiary glycols varied within the range 25-35%. Along with the glycols, intermediate products were formed – diketones and keto alcohols (tertiary). In the case of the esters of the low molecular succinic and oxalic acids, glycols were not obtained, but only the keto alcohols and diketones were formed. The ester of malonic acid reacted with tert-C_4H_9Li by a complex scheme (for which an equation is proposed) with the formation of pinacolin, hexamethylacetone, and di-tert-butylcarbinol.

LITERATURE CITED

1. A. D. Petrov and E. B. Sokolova, Zhur. Obshch. Khim. 8, 199 (1938); A. D. Petrov and P. S. Sanin, Zhur. Obshch. Khim. 8, 195 (1938); 9, 2199 (1939), et al.
2. A. D. Petrov and N. A. Roslova, Zhur. Obshch. Khim. 10, 973 (1940).
3. E. Cadwalader, A. Fookson, T. Mears, and F. Howard, J. of Research Nat. Bur. Stand. 41, 111 (1948).
4. A. E. Favorskii and L. I. Kolotova, Zhur. Russ. Khim. Obshchestva 38, 759 (1906).
5. V. I. Egorova, Zhur. Russ. Khim. Obshchestva 41, 1454 (1909).
6. A. D. Petrov and M. A. Chel'tsova, Doklady Akad. Nauk SSSR 58, 1379 (1947).
7. D. Ivanoff and A. Spasoff, Bull. Soc. Chim. (5), 1, 1419 (1934).
8. H. Gilman, J. Am. Chem. Soc. 63, 2479 (1941).
9. P. D. Bartlett, S. Friedman, and M. Stiles, J. Am. Chem. Soc. 75, 1771 (1953); P. D. Bartlett and E. B. Lefferts, J. Am. Chem. Soc. 77, 2804 (1955).
10. H. Gilman, A. H. Haubein, and H. Hartzfeld, J. Org. Chem. 19, 1034 (1954).
11. K. Ziegler and H. Gellert, Lieb. Ann. 567, 179 (1950).
12. J. B. Conant and A. H. Blatt, J. Am. Chem. Soc. 51, 1236 (1929).
13. F. C. Whitmore and K. C. Laughlin, J. Am. Chem. Soc. 54, 4011 (1932).
14. E. Badertscher and F. C. Whitmore, J. Am. Chem. Soc. 54, 825 (1932).
15. A. E. Favorskii, J. prakt. Chem. (2), 88, 675 (1913).
16. R. Loquin and L. Leers, Compt. rend. 178, 2095 (1924); 179, 55 (1924); Bull. Soc. Chim. (4), 39, 652 (1926).
17. P. W. Clutterbuck and F. Reuter, J. Chem. Soc. (1935), p. 1467.
18. E. Vavon and D. Ivanoff, Compt. rend. 177, 453 (1923).

INVESTIGATIONS IN THE FIELD OF LIPIDS

V. SYNTHESIS OF TRIGLYCERIDES OF PLANT OILS

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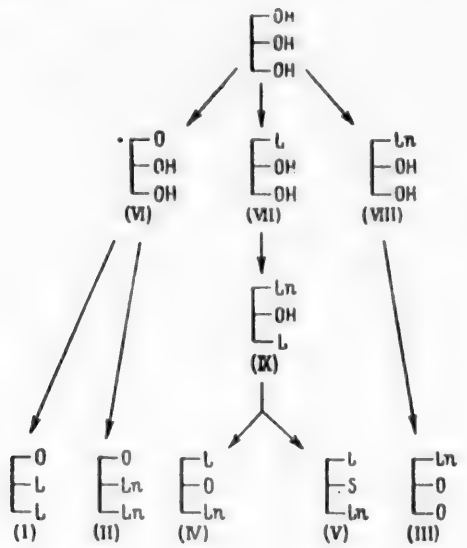
In previous communications [1, 2] we have described the preparation of a series of triglycerides that are components of a number of plant oils: linseed, sunflower, soy, palm, etc. In the present communication, we describe the synthesis and the principal physicochemical properties of other compounds of this type: α-oleyl-β,α'-dilinolein (LLO) (I), α-oleyl-β,α'-dilinolenin (LnLnO) (II), α-linolenoyl-β,α'-dilinolein (LnOO) (III), α-linoleyl-β-oleyl-α'-linolenin (LnOL) (IV), and α-linoleyl-β-stearyl-α'-linolenin (LnSL) (V). The synthesis was carried out by the following scheme.



The triglycerides (I) (LLO) and (II) (LnLnO) were synthesized by the esterification of α-monooleylglycerol (VI) with the chlorides of linoleic and linolenic acids, respectively. The preparation of (III) (LnOO) was carried out in a similar manner, starting with α-monolinolenylglycerol and oleic acid chloride. The mixed triglycerides (IV) (LnOL) and (V) (LnSL) were synthesized from α-monolinoleylglycerol (VII) through α-linolenyl-α'-linoleylglycerol (IX), which was reacted with the chlorides of oleic and stearic acids.

EXPERIMENTAL

α-Oleyl-β,α'-dilinolein (I). To a solution of 12.6 g of α-monooleylglycerol (VI) (m. p. 30-32°, iodine No. 71.5; calc. 71.2) and 9.2 g of quinoline in 60 ml of dry chloroform at 0-3° was added 22 g of linoleic acid

chloride.* The reaction mixture was heated for 4 hours at 58-60° in a current of nitrogen, then cooled to 12-15°, after which 75 ml of ether and 70 ml of 5% sulfuric acid were added. The upper layer that separated out was removed and the compound was extracted from the lower layer with 40 ml of ether. The combined extract was washed with saturated aqueous sodium bicarbonate solution and dried with sodium sulfate. The residue after removal of the solvent was washed with 70 ml of dry methyl alcohol. Twenty-two and six-tenths grams of technical triglyceride was obtained (iodine No. 135.8). For further purification, the material was subjected to fractional crystallization from 113 ml of acetone. At −(25-20)° the precipitate was separated out (1.3 g). The mother liquor was cooled to −(35-30)°. The crystalline precipitate was separated out (13.3 g, iodine No. 140) and for final purification was recrystallized again from 65 ml of acetone at −40 to −35°. Yield 12.4 g (39.79%).

M. p. −14.5 to −13.2°, d^{20}_4 0.9281, $n^{20}D$ 1.4776, MR_D 268.60; Calc. 268.15.

Found %: C 77.96, 77.75; H 11.30, 11.12. Iod. No. 141.6. $C_{57}H_{100}O_6F_5$. Calculated %: C 77.67; H 11.43. Iod. No. 144.0.

α-Oleyl-β,α'-dilinolenin (II). The synthesis was carried out under the conditions used for the preparation of (I), starting with 11.5 g of α-monooleylglycerol (VI) in 55 ml of dry chloroform and 20 g of linolenic acid chloride,** in the presence of 9 g of quinoline. The technical triglyceride (27.5 g) was washed with 60 ml of dry methyl alcohol and a solution of it in 100 ml of acetone was filtered through 10 g of activated carbon, and after the solvent was distilled off, 20.7 g of material was obtained, which was crystallized from 103 ml of acetone. At −32 to −30° the precipitate was separated off (3.1 g, iodine No. 156.8). Then the solid phase (10.8 g, iodine No. 193.5) was filtered off from the mother liquor at −60 to −55° and again crystallized from 54 ml of acetone. The mother liquor after removal of the precipitate (4.4 g, iodine No. 186.3) was cooled to −75 to −70° and the triglyceride (II) was obtained. Yield 5.5 g (19.43%).

M. p. −16 to −14.3°, d^{20}_4 0.9301, $n^{20}D$ 1.4834, MR_D 269.60; Calc. 267.32.

Found %: C 77.80, 77.95; H 10.98, 10.89. Iod. No. 200.5. $C_{57}H_{96}O_6F_7$. Calculated %: C 78.03; H 11.03. Iod. No. 202.5.

α-Linolenyl-β,α'-diolein (III). Eleven and six-tenths grams of α-monolinolenylglycerol (VIII) (d^{20}_4 0.9725, $n^{20}D$ 1.4878, iodine No. 215.3; calc. 215.6) was reacted with 21 g of oleic acid chloride *** in the presence of 50 ml of chloroform and 9.5 g of quinoline. The reaction mixture was heated at 54-56° for 4 hours in a current of nitrogen and after being cooled to 10-15° was diluted with 70 ml of ether and 65 ml of 5% sulfuric acid. The upper layer that separated out was removed, and the compound was extracted from the lower layer with 30 ml of ether. The combined extract was washed with 50 ml of saturated aqueous sodium bicarbonate solution and dried with sodium sulfate. After the solvent was distilled off, 27.8 g of technical triglyceride was obtained, which was washed with 60 ml of methyl alcohol; 25.9 g of the compound was subjected to fractional crystallization from 130 ml of acetone. At −20 to −18° a precipitate separated out (3.4 g, iodine No. 130.6). The mother liquor was cooled to −35 to −30° and the crystalline phase (19.2 g) was removed and again crystallized from 90 ml of acetone at −45 to −40°. Yield 15.2 g (52.40%).

M. p. −12 to −10.4°, d^{20}_4 0.9202, $n^{20}D$ 1.4770, MR_D 270.60; Calc. 268.15.

Found %: C 77.83, 77.38; H 11.20, 11.66. Iod. No. 145.4. $C_{57}H_{100}O_6F_5$. Calculated %: C 77.67; H 11.43. Iod. No. 144.0

α-Linoleyl-β-oleyl-α'-linolenin (IV). The starting material, α-linoleyl-α'-linolenylglycerol (IX) (m. p. −25 to −23.5° and −5.5 to −4.5°, d^{20}_4 0.9423, $n^{20}D$ 1.4851, iodine No. 204.2; calc. 206.4) was synthesized from α-linoleylglycerol and linolenic acid chloride. Eighteen grams of (IX) was reacted with 10 g of oleic acid chloride in the presence of 60 ml of chloroform and 6 g of quinoline. The reaction mixture was heated at 58-60° for 4 hours in a current of nitrogen and after treatment as in the preceding experiments, 25.3 g of the

* B. p. 150-152° at 0.5 mm, d^{20}_4 0.9317, $n^{20}D$ 1.4740, MR_D 89.56. $C_{18}H_{31}OClF_2$. Calculated 89.64.
** B. p. 149-150° at 0.45 mm, d^{20}_4 0.9301, $n^{20}D$ 1.4835, MR_D 91.35. $C_{18}H_{29}OClF_3$. Calculated 89.17.
*** B. p. 148-150° (0.3 mm), d^{20}_4 0.9147, $n^{20}D$ 1.4646, MR_D 90.88. $C_{18}H_{33}OClF$. Calculated 89.74.

technical triglyceride was obtained (iodine No. 155.6). The latter was washed with 60 ml of methyl alcohol and was fractionally crystallized from 120 ml of acetone. The mother liquor, after preliminary removal of the solid fractions at − 35 to − 30° (iodine No. 145.5) and − 40 to − 35° (iodine No. 162.3), was cooled to − 60 to − 55°. The triglyceride obtained in this way was further purified by passing an ether solution of it (1 : 10) through a column with 50 g of aluminum oxide and 10 g of activated carbon. Yield 6 g (23.31%).

M. p. − 29 to − 28°, d^{20}_4 0.9367, $n^{20}D$ 1.4802, MR_D 266.80; calc. 267.59.

Found %: C 77.85, 78.07; H 10.94, 10.93. Iod. No. 171.4. $C_{57}H_{98}O_6$ Fe. Calculated %: C 77.85; H 11.23. Iod. No. 173.2.

α-Linoleyl-β-stearyl-α'-linolenin (V). From 17.5 g of (IX) and 9.5 g of stearic acid chloride in 55 ml of chloroform in the presence of 5.2 g of quinoline was obtained 20.1 g of technical triglyceride (V). To further purify the material it was recrystallized from 100 ml of acetone. The precipitates were separated off successively at − 12 to − 10° and − 20 to − 18°. The compound separated from the mother liquor (iodine No. 157) was recrystallized from acetone at − 60 to − 55° and an ether solution of it (1 : 10) was filtered through a column with 45 g of aluminum oxide. Yield 3.2 g (12.75%).

M. p. − 27 to − 26° and − 10 to − 8.5°, d^{20}_4 0.9239, $n^{20}D$ 1.4793, MR_D 270.7; calc. 268.15.

Found %: C 77.89, 77.97; H 11.04, 11.19. Iod. No. 145.6. $C_{57}H_{100}O_6$ Fe. Calculated %: C 77.67; H 11.43. Iod. No. 144.0.

SUMMARY

1. α-Oleyl-β,α'-dilinolein; α-oleyl-β,α'-dilinolenin; α-linolenyl-β-α'-diolein; α-linoleyl-β-oleyl-α'-linolenin; and α-linoleyl-β-stearyl-α'-linolenin have been synthesized.

2. In the course of the synthesis, along with the principal compounds (triglycerides that are components of a number of plant oils) the following monoglycerides were isolated and characterized by their physicochemical constants: α-oleylglycerol, α-linolenylglycerol, and also the diglyceride α-linolenyl-α'-linoleylglycerol.

LITERATURE CITED

1. M. E. Maurit, I. K. Sarycheva, N. A. Preobrazhenskii, et al., Zhur. Obshch. Khim. 29, 3909 (1959);* O. V. Utkina, M. E. Maurit, I. K. Sarycheva, and N. A. Preobrazhenskii, Zhur. Obshch. Khim. 29, 3911 (1959).*
2. I. K. Sarycheva, O. V. Utkina, M. E. Maurit, G. A. Vorob'eva, M. N. Vargaftik, N. A. Krit, A. I. Sherle, N. A. Preobrazhenskii, et al., Zhur. Obshch. Khim. 29, 3583 (1959).*

* Original Russian pagination. See C. B. translation.

SYNTHESIS OF THE METHYL ESTER OF TROPANONE-3-CARBOXYLIC-2 ACID

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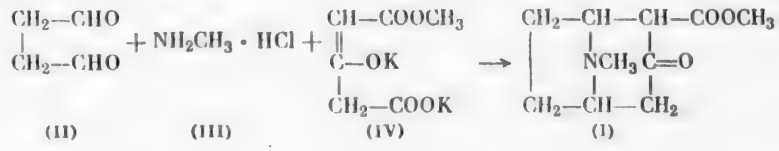
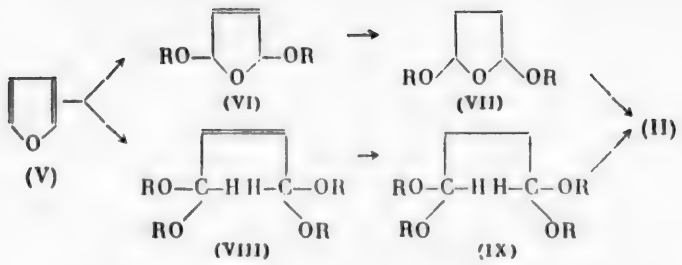
The main intermediate product in the synthesis of the alkaloid cocaine is the methyl ester of tropanone-3-carboxylic-2 acid (I). In our previous communications [1, 2] we have described a method of preparing this ester that is based on the condensation of succinic dialdehyde (II) with methylamine hydrochloride (III) and the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (IV). This route was proposed by Willstätter, et al. [3] in 1932.



(II) (III) (IV) (I)

However, wide use of the reaction has been hindered by the absence of suitable methods for the synthesis of succinic dialdehyde (II). It became practicable only in recent years, when Clauson-Kaas [4, 5] and other authors [6, 7] suggested furan (V) as a raw material for the synthesis of succinic dialdehyde. In the literature a whole series of methods is described for the preparation of succinic dialdehyde (II). Most of the methods are mainly of theoretical interest, because of the low yields, experimental difficulties, or the absence of available raw materials, while the preparation of succinic dialdehyde from furan is rather simple and can be employed in practice. Furan (V) at low temperatures [6] reacts with chlorine (or bromine) and alcohol to give 2,5-dialkoxy-2,5-dihydrofuran (VI). It is reduced to 2,5-dialkoxytetrahydrofuran (VII), which can be considered as a cyclic acetal of succinic dialdehyde and from which succinic dialdehyde (II) is obtained by acid hydrolysis. In the investigations that have been published on this problem [1, 2, 4, 5, 7], yields of 55 to 80% were obtained for the stage of the preparation of (VI), but no other reaction products were mentioned. Only Clauson-Kaas [5] states that in the vat residue after distillation of the 2,5-dialkoxy-2,5-dihydrofuran (VI) he found a small amount of a material that was identified in the form of the bis-semicarbazone as the acetal of maleic dialdehyde (VIII). The possibility of breaking the furan ring with a methanol solution of hydrogen chloride by heating in sealed tubes was described by Harries [8], who obtained in this way, however, the acetal, not of maleic dialdehyde (VIII), but of succinic dialdehyde (IX).

Taking into account the technological difficulties of carrying out low-temperature processes, we studied the methoxylation reaction at temperatures from − 40 to − 35° to − 12 to − 10° and found that, besides the already well-known reaction of formation of 2,5-dimethoxy-2,5-dihydrofuran (VI), we observed the formation of products that originated from the opening of the furan ring by acid agents. Thus, we isolated the methyl diacetal of maleic dialdehyde (VIII) and some halogen-containing products and, in contrast to Harries [8], we showed that the formation of (IX) can go not in one stage, but through the compound (VIII), which contains a double bond.



Carrying out the methoxylation at − 12 to − 10° leads to opening of the furan ring and formation, along with the cyclic acetal (VI), of the open acetal (VIII). For example, at −40 to −35° only 2,5-dimethoxy-2,5-dihydrofuran is formed, but at − 12 to −10° we obtained 14.9% of 2,5-dimethoxy-2,5-dihydrofuran (VI) and 44.2% of the methyl diacetal of maleic dialdehyde (VIII). In the case of methoxylation at 0°, a larger amount of high-boiling materials containing halogen was observed and we did not succeed in isolating compound (VI).

In addition to temperature, the concentration of the reacting compounds plays an important role in the alkoxylation reaction, since when the volume of the reaction mixture is decreased and the concentration of the acid halide is increased the reaction is too violent and leads to opening of the ring. The use of increased amounts of alcohol or other solvents permits carrying out the alkoxylation at −12 to −10° and avoiding the formation of halogenated products.

The methyl diacetal of maleic dialdehyde (VIII) was hydrogenated in the presence of Raney nickel at a pressure of 5-7 atm. The yield of the methyl diacetal of succinic dialdehyde was 90.9%. The diacetal of succinic dialdehyde (IX) that was obtained was condensed with methylamine hydrochloride and the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid in the presence of acetate buffer and the methyl ester of tropanone-3-carboxylic-2 acid (I) was obtained.

We also investigated the electrochemical alkoxylation of furan in the presence of ammonium bromide (chloride) in alcohol medium under different conditions. The 2,5-dialkoxytetrahydrofuran and the diacetal of succinic dialdehyde that were obtained proved to be identical with those synthesized by chemical methods.

EXPERIMENTAL

1. 2,5-Dimethoxy-2,5-dihydrofuran (VI, R = CH_3). a) Seventy grams of dry chlorine was passed, in the course of 1 hour, with stirring, into a solution of 68 g of furan in 630 ml of anhydrous methyl alcohol and 630 ml of dry methylene chloride cooled to − 40° to −35°, or else 159.9 g of bromine dissolved in 630 ml of dry methylene cooled to − 40° was added dropwise to the furan solution, in which case the furan was dissolved in 630 ml of anhydrous methyl alcohol. The addition was made at such a rate that the temperature of the reaction mixture did not exceed − 25°. After 30 minutes stirring at the same temperature a current of dry ammonia was passed in until a pH of 8 was reached. After the neutralization was completed, the precipitate that had separated out was filtered off and washed with methylene chloride (3 times with 50 ml portions). The residue after the solvent was distilled off (127.8 g) was distilled. The product was a colorless liquid, readily soluble in ether, benzene, chloroform, and other organic solvents. Yield 90.1 g (69.3%).

B. p. 39-41° (4 mm), d^{20}_4 1.0697, $n^{20}D$ 1.4349, $n^{25}D$ 1.4325, MR_D 31.74; calc. 32.17.

Found %: C 55.51; H 7.86. $C_6H_{10}O_3$. Calculated %: C 55.37; H 7.74.

b) The compound was prepared in a similar manner with the difference that the alkoxylation was carried out in anhydrous methyl alcohol. Yield 93.9 g (72.2%).

B. p. 35-37° (3 mm), 39-42° (4 mm), 60-62° (15 mm), d^{20}_4 1.0684, $n^{20}D$ 1.4347, $n^{25}D$ 1.4325, MR_D 31.76; calc. 32.17.

2. Methyl diacetal of maleic dialdehyde (VIII, R = CH_3). A solution of 159.9 g of bromine in 700 ml of anhydrous methyl alcohol cooled to − 15° was added dropwise, with stirring, to a solution of 68 g of furan

(b. p. 31.5-32° at 756 mm, d^{20}_4 0.934, $n^{20}D$ 1.4200) in 500 ml of anhydrous methyl alcohol cooled to −12°. The addition was made at such a rate that the temperature of the reaction mixture did not exceed −10 to −8° (about 1 hour). After 20 minutes stirring at the same temperature, a current of dry ammonia was passed into the reaction mixture until the pH reached 8 (about 1 hour). The methyl alcohol was distilled off at 20-25° in a vacuum of 20-25 mm. The precipitate that had separated out was filtered off and washed with 290 ml of methylene chloride. The residue after the solvent was distilled off was distilled. Two fractions were obtained: 1st – 2,5-dimethoxy-2,5-dihydrofuran, yield 19.4 g (14.9%), b. p. 34-45° (3 mm), 68-75° (15 mm); 2nd – methyl diacetal of maleic dialdehyde, yield 74.8 g (44.2%). The latter product was a colorless liquid, readily soluble in ether, benzene, chloroform, and other organic solvents.

B. p. 53-58° (3 mm), 88-90° (15 mm), d^{20}_4 1.0102, $n^{20}D$ 1.4292, MR_D 44.99; calc. 45.25.

Found %: C 54.67, 54.77; H 9.32, 9.31; OCH_3 70.37. $C_8H_{16}O_4$. Calculated %: C 54.52; H 9.15; OCH_3 70.44.

3. Methyl diacetal of succinic dialdehyde (IX, R = CH_3). Twenty-five grams of the methyl diacetal of maleic dialdehyde was hydrogenated in the presence of 6 g of Raney nickel catalyst at room temperature and atmospheric pressure with mechanical stirring. After 3.3 liters of hydrogen had been absorbed in about 3.5 hours (3.32 liters of hydrogen is required for 25 g of the methyl diacetal), the catalyst was filtered off and washed with 10 ml of anhydrous methyl alcohol. The residue after the solvent had been distilled off was distilled. The product was a colorless liquid, readily soluble in ether, toluene, chloroform, and other organic solvents. Yield 23 g (90.9%).

B. p. 77-79° (9 mm), d^{20}_4 0.9875, $n^{20}D$ 1.4153, MR_D 45.22; calc. 45.71.

Found %: C 53.65, 53.73; H 9.86, 10.14; OCH_3 69.97. $C_8H_{16}O_4$. Calculated %: C 53.91; H 10.18; OCH_3 69.65.

Diphenylhydrazone of succinic dialdehyde. Four and two-tenths ml of hydrochloric acid (d 1.18) and 46 ml of water were heated to 80°, 6 g of the methyl diacetal of succinic dialdehyde was added, and the mixture was stirred at 80° for 20 minutes. The mixture was cooled and the volume brought to 60 ml, 10 ml of the solution was neutralized with potassium carbonate solution (at 0°) and 1.3 g of phenylhydrazine in 20 ml of water was added. Several drops of acetic acid were added. Yield 1.4 g (93.8%). M. p. 114-115° (from alcohol).

Found %: N 21.46. $C_{16}H_{18}N_4$. Calculated %: N 21.03.

4. Methyl ester of tropanone-3-carboxylic-2 acid (I). To 90 ml of 1 N hydrochloric acid, heated to 80°, was added 11 g of the methyl diacetal of succinic dialdehyde and the mixture was stirred at the same temperature for 20 minutes. The reaction mixture was cooled rapidly to 0°, after which there were added to it in succession 20.3 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (IV), 65 ml of 12% aqueous sodium acetate solution, and 5.8 g of methylamine hydrochloride (III). The mixture obtained was stirred at 30° for 4 hours. The reaction mixture was cooled to 0°, saturated with 80 g of potassium carbonate, and extracted with benzene (4 times with 80 ml portions). The residue after the solvent was distilled off was distilled. Yield 7.2 g (59.2%). B. p. 92-95° (0.3 mm), m. p. 101-103°.

Found %: C 60.62; H 7.54; N 6.95. $C_{10}H_{15}O_3N$. Calculated %: C 60.87; H 7.66; N 7.09.

SUMMARY

1. The action of chlorine (bromine) and methyl alcohol on furan has been studied and it has been shown that carrying out the reaction at − 40 to − 35° leads to the formation of 2,5-dimethoxy-2,5-dihydrofuran, but at − 12 to − 10° the reaction proceeds with the opening of the ring and the formation of the methyl diacetal of maleic dialdehyde; at a higher temperature a mixture of high-boiling materials containing halogen is produced.

2. The hydrogenation of the methyl diacetal of maleic dialdehyde to the methyl diacetal of succinic dialdehyde has been carried out.

3. A method has been developed for the synthesis of the methyl ester of tropanone-3-carboxylic-2 acid from the diacetal of succinic dialdehyde, methylamine hydrochloride, and the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid.

LITERATURE CITED

1. G. I. Bazilevskaya, D. V. Gura, M. S. Bainova, K. M. Dyumaev, I. K. Sarycheva, and N. A. Preobrazhenskii, Zhur. Obshch. Khim. 28, 1097 (1958).*
2. G. I. Bazilevskaya, M. S. Bainova, D. V. Gura, K. M. Dyumaev, and N. A. Preobrazhenskii, Izvestiya Vyssh. Shkol. Khimia i Khim. Tekhnol. 1, 76 (1958).
3. R. W. Willstätter, O. Wolfes, and H. Mäder, Lieb. Ann. 434, 111 (1923).
4. N. Clauson-Kaas, Kgl. Danske Videnskab. Salskab., Mat. fys. Medd. 24, 6 (1947); N. Clauson-Kaas, F. Limborg, and J. Fakstorp, Acta Chim. Scand. 2, 109 (1948).
5. N. Clauson-Kaas, F. Limborg, and K. Glens, Acta Chem. Scand. 6, 531 (1952); Danish patent 80,900; 78,456.
6. British patent 595,041; Chem. Abstract 42, 2992 (1948).
7. J. Fakstorp, D. Raleigh, and L. E. Schniepp, J. Am. Chem. Soc. 72, 869 (1950); D. L. Hufford, D. S. Tarbell, and T. R. Koszalka, J. Am. Chem. Soc. 74, 3014 (1952).
8. C. Harries, Ber. 31, 37 (1898); A. Wohl and E. Berenther, Lieb. Ann. 481, 1 (1930).

*Original Russian pagination. See C.B. translation.

INVESTIGATIONS IN THE FIELD OF SULFONES AND SULFOXIDES

I. VINYL ETHYL SULFONE, ITS SYNTHESIS AND SOME CONVERSIONS

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Vinyl sulfones have an active double bond, which readily adds reagents of the type HX (alcohols, mercaptans, amines, water, etc.) under the influence of various alkaline catalysts to form products in which the nucleophilic group X goes on to the end carbon atom of the double bond. A large part of the reactions are described in patents and in examples either of divinyl sulfone [1] or of substituted aryl vinyl sulfones, and particularly of the higher members of the alkyl vinyl sulfones [2]. The reactions of the lower alkyl vinyl sulfones have received very little study. It has been reported [3] that vinyl methyl, butyl, and isobutyl vinyl sulfones in alkaline medium readily add nitroparaffins. Vinyl methyl sulfone undergoes condensation of the Mikhaelev type with compounds having an active methylene group [4], and vinyl ethyl sulfone reacts with thiols in the presence of triethylamine [5]. It is known that vinyl methyl sulfone [6] (in contrast to the substituted vinyl aryl sulfones [7]) readily enters into a diene condensation with cyclopentadiene, butadiene, methyl- and dimethylbutadiene. There are indications (patent) of water-emulsion polymerization and joint polymerization of alkyl vinyl sulfones in the presence of salts of peracids with the formation of substances useful as auxiliary agents in the textile industry, and also as benzene-resistant rubbers [8]. In the case of condensation in the presence of alkaline agents with methylene groups in their molecules, oily or rubbery polymers are produced [9]. Price, et al. [10], found that in the presence of benzoyl peroxide the vinyl methyl and phenyl sulfones show a low monomer activity in joint polymerization reactions with vinyl acetate and styrene.

From the existing data, it is difficult to form a clear picture of the reactivity of the lower vinyl alkyl sulfones (for which these rules should emerge especially clearly) under conditions of initiation both by ions and by free-radical initiators. The present investigation was begun for the purpose of filling this gap and vinyl ethyl sulfone was selected as the starting material. We synthesized it by the dehydration of 2-hydroxydiethyl sulfone (I) over phosphoric acid at 260-270° in vacuo, i.e., under the conditions recently suggested for the preparation of divinyl sulfone from β,β'-dihydroxydiethyl sulfone [11].

$$HOCH_2CH_2SC_2H_5 \xrightarrow{H_2O_2} \underset{(I)}{HOCH_2CH_2SO_2C_2H_5} \xrightarrow{H_3PO_4} \underset{(II)}{CH_2{=}CHSO_2C_2H_5}$$

This method makes it possible to obtain a rather high yield (70-75%) of pure vinyl ethyl sulfone (II) without any contamination by sulfoxides.* In this respect, it is considerably more convenient than the method of synthesis

* If the 2-hydroxydiethyl sulfone itself, which is obtained by the oxidation of 2-hydroxydiethyl sulfide, contains the corresponding sulfoxide, it is destroyed in the dehydration process.

based on the oxidation of vinyl sulfides, in which it is difficult to avoid contamination by vinyl sulfoxide [12]. The dehydration method also has significant advantages over the dehydrochlorination of β-chloroethyl alkyl sulfones that has frequently been used by various authors [1, 2a, 3, 4, 6, 10], especially if we take into account that in the latter case toxic semi-mustard gases are used as starting materials.

$$HOCH_2CH_2SR \xrightarrow{HCl} ClCH_2CH_2SR \xrightarrow{H_2O_2} ClCH_2CH_2SO_2R \xrightarrow{-HCl} CH_2{=}CHSO_2R.$$

For the initiation of ionic reactions of vinyl ethyl sulfone (II) we used Triton B.* Under its influence the addition of various reagents is accomplished especially easily, in most cases quantitatively and with a considerable elevation in temperature.

$$C_2H_5SO_2CH{=}CH_2 \;(II) \begin{cases} \xrightarrow{C_6H_5SH} C_2H_5SO_2CH_2CH_2SC_6H_5 & (III) \\ \xrightarrow{C_2H_5OH} C_2H_5SO_2CH_2CH_2OC_2H_5 & (IV) \\ \xrightarrow{H_2O} C_2H_5SO_2CH_2CH_2OH & (I) \end{cases}$$

These reactions apparently have an anion-chain mechanism. The addition products are formed in high yields if the catalyst is introduced into an equimolar mixture of the starting materials. If, however, the catalyst is introduced into previously cooled compound (II) and the second reagent is then added to it, a considerable amount of a low-molecular polymer of (II) is formed along with the addition product. We showed in a special experiment that Triton B produces quantitative polymerization of (II) at room temperature in 20 hours. The rules that have been mentioned can be explained by the competition in the anion-chain process between the polymerization and the addition reactions according to the equations:

$$(CH_3)_3\overset{+}{N}CH_2C_6H_5\,\overline{OH} + CH_2{=}CHSO_2C_2H_5 \rightarrow HOCH_2\overline{C}HSO_2C_2H_5 + (CH_3)_3\overset{+}{N}CH_2C_6H_5$$

(initiation of polymerization)

$$(CH_3)_3\overset{+}{N}CH_2C_6H_5\,\overline{OH} + HX \rightarrow (CH_3)_3\overset{+}{N}CH_2C_6H_5 + H_2O + X^-.$$

(formation of ion-initiator for addition)

$$HOCH_2\overline{C}HSO_2C_2H_5 + CH_2{=}CHSO_2C_2H_5 \rightarrow HOCH_2{-}\underset{\displaystyle SO_2C_2H_5}{\underset{|}{CH}}{-}CH_2\overline{C}HSO_2C_2H_5 \text{ (etc.)}$$

(growth of polymerized chain)

$$HO[CH_2CH(SO_2C_2H_5)]_nCH_2\overline{C}HSO_2C_2H_5 + HX \rightarrow$$
$$\rightarrow HO[CH_2CH(SO_2C_2H_5)]_nCH_2CH_2SO_2C_2H_5 + X^-$$

(interruption of polymerization with simultaneous formation of ion-initiator for addition)

$$X^- + CH_2{=}CHSO_2C_2H_5 \rightarrow XCH_2\overline{C}HSO_2C_2H_5$$

(initiation of addition)

$$XCH_2\overline{C}HSO_2C_2H_5 + HX \rightarrow XCH_2CH_2SO_2C_2H_5 + X^- \text{ (etc.)}$$

(anion-chain addition)

We may cite as an example the addition of thiophenol. When the catalyst was introduced into an equimolar mixture of the reagents, 90-95% of 1-ethylsulfonyl-2-phenylmercaptoethane (III) was formed, but when the reaction was carried out by the second method, up to 25% of the trimer (II) was obtained along with 70% of (III).

It is interesting to compare these results with the data of Karasch [14], who found that when he added mercaptans to methyl acrylate in the presence of Triton B there was quantitative formation of addition products; in the presence of free-radical initiators (ascaridol, light) a mixture of telomeric compounds was formed. The different behavior of the systems acrylate – mercaptan and sulfone – mercaptan is associated, apparently, with

* After we had completed most of our experiment, the use of Triton B as a catalyst for addition of ethyl mercaptan to vinyl ethyl sulfone was reported in the literature [13].

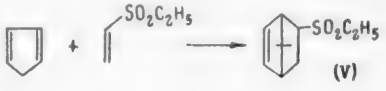
the fact that the vinyl sulfone molecule enters into anion polymerization considerably more readily and into free-radical polymerization with more difficulty than the acrylate molecule.

In free-radical addition reactions we have not yet succeeded in achieving appreciable activity of the vinyl sulfone molecule. When an equimolar mixture of thiophenol and (II) stood in the air for 3 weeks or was heated for a long time in the presence of azoisobutyrodinitrile, there was practically no formation of addition products (while, for example, vinyl alkyl sulfides form addition products with mercaptans with spontaneous evolution of heat upon simply being mixed in the air [15]). Prolonged heating of (II) in the presence of free-radical initiators leads, however, to the formation of considerable amounts of polymers (see table).

Polymerization of Vinyl Ethyl Sulfone (60°, 60 hours)

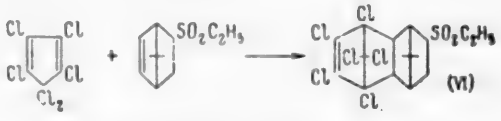
Initiator (%)	Yield of polymer (in %)	$n^{20}D$ of polymer	Solubility of Polymer			
			water	C_2H_5OH	C_6H_6	petroleum ether
Azoisobutyrodinitrile, 0.2	63.6	1.5068	+	+	–	–
Benzoyl Peroxide, 0.2	59.3	1.5005	+	+	–	–
	15.4	1.4650	+	+	–	Slight

Finally, we investigated the behavior of (II) in the diene synthesis and were convinced of its very high dienophilic activity. Thus, with cyclopentadiene it readily formed 2-bicyclo[2.2.1]hepten-5-yl ethyl sulfone (V) (quantitative yield, reaction accompanied by spontaneous evolution of heat).



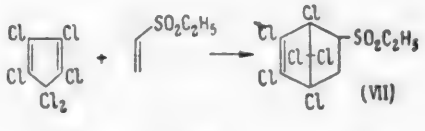
(V)

In this process not even traces of products of further condensation at the bicycloheptene double bond were formed. At higher temperatures, however, this double bond also may be utilized. Thus, with hexachlorocyclopentadiene the compound 2-ethylsulfonyl-5,6,7,8,10,10-hexachloro-1,4,5,8-diendomethylen-1,2,3,4,4a,5,8,8a-octahydronaphthalene (VI) was produced (yield 50%).

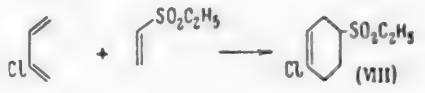


(VI)

With hexachlorocyclopentadiene and chloroprene compound (II) also readily formed the corresponding adducts (VII) and (VIII) (yields 82 and 65%, respectively).



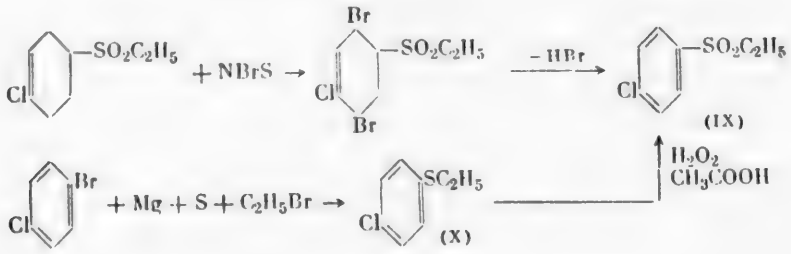
(VII)



(VIII)

In the latter case, apparently in a manner similar to other diene condensations of chloroprene [16], the predominant product was ethyl-4-chloro-$\Delta^{3,4}$-cyclohexenyl sulfone (VIII). We proved this by the aromatization

of the adduct obtained by brominating it with N-bromosuccinimide and subsequently dehydrating in pyridine, as described in the literature for the dehydration of other cyclohexene systems [17, 18]. The product obtained did not give any depression in melting point with known p-chlorophenyl ethyl sulfone synthesized from p-chlorobromobenzene.



All the adducts of the bicycloheptene series have C=C frequencies corresponding to these systems in the infrared spectra and the Raman spectra.

The data presented here indicate that the SO_2 group is a strong electron-drawing group which activates the double bond both in reactions of the anion type and in such conversions as the diene synthesis, where the high polarity of the double bond favors the conversion. Reactions of a free-radical nature apparently are not very characteristic of this class of compounds.

EXPERIMENTAL

2-Hydroxydiethyl sulfone (I). To 106.2 g (1 mole) of 2-hydroxydiethyl sulfide (b. p. 79-80° at 15 mm, $n^{20}D$ 1.4252) containing 2% of H_3PO_4 was added 236 ml of 29.4% H_2O_2 (2.02 moles) at such a rate that the temperature of the reaction mixture did not exceed 70°, after which the solution was refluxed until there was a negative test for the presence of peroxide. The water was distilled off in vacuum and the residue crystallized upon cooling. The yield of (I) was quantitative, 138.2 g. White hygroscopic crystals with m. p. 42.5-43° (from ethyl acetate); the product did not distill without decomposition under a vacuum of 3 mm.

Found %: C 34.76; H 7.46; S 22.94. $C_4H_{10}O_3S$. Calculated %: C 34.76; H 7.49; S 23.20.

Dehydration. Seventy grams of crystalline H_3PO_4 was placed in a 500-ml three-necked flask fitted with a dropping funnel, thermometer, capillary, a headpiece connected with a descending condenser, and refrigerated traps. The acid was freed of water by heating to 300° at 15-20 mm; the fused material was cooled to 270° and to it was slowly added 112 g of melted (I) (b. p. 270-280° at 10-12 mm). The reaction was carried out in a current of nitrogen. From the homogeneous mixture of vinyl ethyl sulfone (II) and water that was obtained, the latter was distilled off in vacuum and the residue was dried over Na_2SO_4 and distilled. Yield of (II) 83.7 g (74.7%), b. p. 97-98° at 5 mm, $n^{20}D$ 1.4640, d^{20}_4 1.1457. (The constants agreed with the literature data [2]). The absence of a characteristic maximum at 247 mμ in the UV spectrum [12] indicated that the (II) did not contain any traces of sulfoxide.

1-Ethylsulfonyl-2-phenylmercaptoethane (III). a) To a mixture of 3.3 g (0.0275 mole) of (II) and 3 g (0.0275 mole) of thiophenol was added one drop (0.03 g) of Triton B in the form of a 40% aqueous solution. The temperature immediately began to rise sharply. The reaction mixture was cooled with ice water and left for 3 hours at room temperature. On distillation, 5.9 g (90.1%) of (III) was obtained with b. p. 124-125° at 0.04 mm, $n^{20}D$ 1.5751; after cooling with dry ice the compound crystallized in slightly hygroscopic crystals with m. p. 39-40° (from heptane); in [5] the m. p. 36-38° is given.

Found %: C 52.05; H 6.02; S 27.68; $C_{10}H_{14}O_2S$. Calculated %: C 52.14; H 6.12; S 27.90.

b) To 6 g (0.05 mole) of (II), cooled with ice and salt, was added 0.15 g of a 40% aqueous solution of Triton B (abrupt darkening and rise in temperature to +15°), and then, with the temperature of the mixture not higher than 35-40°, 5.5 g (0.05 mole) of thiophenol was added drop by drop. The viscous, light yellow product was heated for 2 hours at 45-50°. The next day, distillation yielded 8.1 g (70.2%) of (III) with b. p. 128-130° at 0.05 mm and 2.0 g of a compound with b. p. 184-186° at 0.04 mm, $n^{20}D$ 1.5213, soluble in benzene, and solidifying to a glassy mass upon cooling with dry ice.

Found %: S 25.75. M 340. $C_{10}H_{20}O_6S_2$. Calculated %: S 25.40. M 378.5.

c) To a mixture of 4.5 g (0.0412 mole) of thiophenol and 5.0 g (0.041 mole) of (II) was added several mg of azoisobutyrodinitrile and the mixture was heated in a sealed ampoule, previously blown out with nitrogen, for 18 hours on a boiling water bath. After the unreacted products had been distilled off, 0.5 g (5%) of (III) was obtained with b. p. 124-125° at 0.05 mm, m. p. 39-40°, which gave no depression in melting point with the product obtained in the presence of Triton B.

1-Ethylsulfonyl-2-ethoxyethane (IV). To 3 g (0.025 mole) of (II) dissolved in 3 ml of anhydrous ethanol was added one drop of Triton B. The temperature rose sharply, the reaction mixture was cooled with cold water and left overnight. The next day, distillation yielded 3.8 g (90.6%) of (IV).

B. p. 125-128° at 4 mm, $n^{20}D$ 1.4518, d^{20}_4 1.1142, MR_D 40.2; calc. 40.13.

Found %: C 43.40; H 8.41; S 19.30. $C_6H_{14}O_3S$. Calculated %: C 43.49; H 8.49; S 19.29.

Hydration of (II). To 3 g (0.025 mole) of (II) dissolved in 50 ml of water was added 3 drops of catalyst. The reaction mixture was heated for 4 hours at 80-90°, after which the excess water was evaporated in vacuum. The residue crystallized upon cooling. Three and one-tenth grams of (I) (90%) was obtained. After recrystallization from ethyl acetate the m. p. was 42-43° (no depression in melting point with the starting 2-hydroxydiethyl sulfone). When the hydration was carried out in the presence of a smaller amount of water, then a polymer of (II) was obtained along with (I).

Polymerization of (II). a) In the presence of Triton B. To 6 g of (II) was added, at room temperature, 2 drops of Triton B (1% solution or 0.4% of active ingredient); the temperature immediately began to rise and the mixture slowly thickened. In 20 hours all of it had solidified to a dark brown thick mass. After the monomer had been removed in a vacuum of 10^{-2} mm, the weight of the polymer was 5.5 g (90%).

b) In the presence of free-radical initiators the polymerization was carried out in sealed ampoules, previously blown out with nitrogen, in a thermostat at 60 ± 0.1° (60 hours). The polymers were freed of monomer by heating to 60° at 10^{-2} mm to constant weight in a current of nitrogen. The properties of the polymers are given in the table. The results of analysis of the polymer obtained in the presence of azoisobutyrodinitrile were as follows:

Found %: C 39.86; H 6.73; S 26.36. $(C_4H_8O_2S)_n$. Calculated %: C 40.00; H 6.60; S 26.60.

2-Bicyclo[2.2.1]hepten-5-yl ethyl sulfone (V). To 6 g (0.05 mole) of (II) containing several mg of hydroquinone was added 4 g (0.05 mole) of freshly distilled cyclopentadiene. The temperature slowly rose to 50° and the mixture became viscous. After 4 days, distillation yielded 8.4 g of (V) (90.6%).

B. p. 70° at 0.01 mm, $n^{20}D$ 1.5135, d^{20}_4 1.1892, MR_D 47.12; calc. 47.45.

Found %: C 58.14; H 7.78; S 17.43. $C_9H_{14}O_2S$. Calculated %: C 58.02; H 7.57; S 17.21.

In the IR spectrum characteristic frequencies were found for the sulfone group at 1140 cm^{-1} (intense) and for the bicycloheptene double bond at 1570 cm^{-1} (weak), and in the Raman spectrum an intense frequency of 1570 cm^{-1} was found.*

(V) under the usual conditions [7] gave a hydrotriazole with phenyl azide, which after chromatography in benzene solution on Al_2O_3, evaporation of the benzene, washing of the oil that was obtained with petroleum ether, and drying, had a m. p. of 38-40°.

Found %: N 13.96. $C_{15}H_{19}O_2N_3S$. Calculated %: N 13.76.

2-Ethylsulfonyl-5,6,7,8,10,10-hexachloro-1,4,5,8-diendomethylen-1,2,3,4,4a,5,8,8a-octahydronaphthalene (VI). To 15 g (0.081 mole) of (V) were added 17.2 g (0.081 mole) of freshly distilled hexachlorocyclopentadiene and several mg of hydroquinone. The mixture was heated at 120-130° in a flask with a reflux condenser (20 hours).

* All of the spectra were determined in the laboratory of the Institute of Organic Chemistry by T. N. Shkurina (deceased) and B. V. Lopatin, for which the authors express their thanks.

(VI) was precipitated from the reaction mixture with methanol. Yield 16 g (49.7%); after recrystallization from alcohol, m. p. 162°. In the IR spectrum characteristic frequencies were found at 1572 and 1148 cm^{-1}.

Found %: C 36.92; H 2.98; S + Cl 52.83. $C_{14}H_{14}O_2SCl_6$. Calculated %: C 36.64; H 3.07; S + Cl 53.32.

2-Ethylsulfonyl-1,4,5,6,7,7-hexachlorobicyclo[2.2.1]heptene-5 (VII). Six grams (0.05 mole) of (II) and 13.7 g (0.05 mole) of freshly distilled hexachlorocyclopentadiene were mixed in a flask with a reflux condenser. The temperature of the reaction mixture rose to 40°. The mixture was heated on a glycerol bath at 140-150° (16 hours). After the first crystallization from carbon tetrachloride 16.2 g (82%) of (VII) was obtained. After repeated crystallization the m. p. was 65-66°. Characteristic frequencies were found in the IR spectrum at 1575 and 1150 cm^{-1}.

Found %: C 27.46; H 19.8; S 8.25; Cl 53.99. $C_9H_8O_2SCl_6$. Calculated %: C 27.5; H 2.05; S 8.16; Cl 54.12.

Ethyl-4-chloro-$\Delta^{3,4}$-cyclohexenyl sulfone (VIII). In an ampoule that had been blown out with nitrogen was placed a mixture of 4.4 g of chloroprene (0.05 mole), 12 g of (II) (0.1 mole), and several mg of pyrogallol. The ampoule was heated for 2 hours at 140-150° (in a protective casing). Upon distillation, 6.8 g (65.4%) of (VIII) was obtained with b. p. 101-102° at 0.01 mm; the product crystallized when cooled with dry ice. M. p. 59-61° (from water).

Found %: C 46.41; H 6.42; S + Cl 32.20. $C_8H_{13}O_2SCl$. Calculated %: C 46.03; H 6.28; S + Cl 32.35.

For the aromatization of (VIII) a solution of 5.5 g of N-bromosuccinimide, 2.8 g of (VIII), and several mg of benzoyl peroxide in 60 ml of benzene was refluxed for 10 hours. The mixture was cooled, the succinimide (quantitative yield) was filtered off, and the benzene was evaporated in vacuum. While the residue was cooled with a mixture of ice and salt, 3.5 g of freshly distilled pyridine (3:1 ratio to the adduct) was added carefully from a dropping funnel. The darkened mixture was diluted with ether and washed with 30 ml of 10% HCl. The ether layer was separated, washed twice with saturated sodium carbonate solution and with water, and dried with calcined sodium sulfate. The ether was distilled off and the residue was dissolved in benzene and chromatographed on Al_2O_3. After the benzene had been evaporated and the product had been crystallized from petroleum ether, 2.1 g (75%) of (IX) was obtained with m. p. 35-37°.

Found %: C 46.75; H 4.32; S 15.67; Cl 17.59. $C_8H_9O_2SCl$. Calculated %: C 46.93; H 4.43; S 15.67; Cl 17.32.

Confirmatory synthesis of (IX). p-Chlorophenyl ethyl sulfide (X) was prepared in 25% yield from p-chlorobromobenzene by Bodroux's method [19]. (X) has not been described in the literature.

B. p. 95-97° at 3 mm, $n^{20}D$ 1.5784, d^{20}_4 1.1688, MR_D 49.05; calc. 48.93.

Found %: C 55.57; H 5.26; S 18.50; Cl 20.64. C_8H_9SCl. Calculated %: C 55.63; H 5.26; S 18.57; Cl 20.53.

(X) was oxidized by the method of [20]. From 2.1 g of (X) in 10 ml of acetic acid and 6 ml of 30% hydrogen peroxide we obtained 1.8 g (72%) of (IX); after two recrystallizations from petroleum ether the m. p. was 35-37°. The product gave no depression in melting point with p-chlorophenyl ethyl sulfone obtained by the aromatization of (VIII).

Found %: C 47.26; H 4.40; S 15.63; Cl 17.14. $C_8H_9O_2SCl$. Calculated %: C 46.93; H 4.43; S 15.67; Cl 17.32.

SUMMARY

1. A convenient method has been suggested for the preparation of vinyl ethyl sulfone by dehydration of 2-hydroxydiethyl sulfone in vacuum over phosphoric acid.

2. It has been shown that Triton B is a universal catalyst which makes it possible to add alcohols, mercaptans, and water easily to the vinyl sulfone, and also to polymerize the sulfone.

3. A test polymerization of vinyl ethyl sulfone has been carried out under the influence of free-radical initiators and its polymers have been prepared in considerable yields (on prolonged heating).

4. The high dienophilic activity of vinyl ethyl sulfone has been shown and its adducts with cyclopentadiene, hexachlorocyclopentadiene, and chloroprene have been prepared.

LITERATURE CITED

1. C. Suter, Chemistry of Organic Compounds of Sulfur [Russian translation] (IL, Moscow, 1951), Part III.
2. a) C. E. Schildknecht, Vinyl and Related Polymers (1952), p. 639; b) W. Reppe, et al., Lieb. Ann. 601, 81 (1956).
3. G. D. Buckley, J. L. Charlich, and J. Rose, J. Chem. Soc. (1947), p. 1544.
4. W. E. Truce and E. Wellisch, J. Am. Chem. Soc. 74, 2888 (1954).
5. A. H. Ford-Moore, J. Chem. Soc. (1949), p. 2433.
6. H. Snyder, H. Anderson, and D. Hallada, J. Am. Chem. Soc. 73, 3285 (1951).
7. K. Alder, H. Rickert, and E. Windemuth, Ber. 71B, 2451 (1938).
8. U. S. Patent 2,472,672 (1949); Chem. Abs. 43, 7266 (1949).
9. U. S. Patent 2,493,364 (1950); Chem. Abs. 44, 5643 (1950).
10. C. C. Price and R. G. Gillis, J. Am. Chem. Soc. 73, 4750 (1951); C. C. Price and J. Zomlefer, J. Am. Chem. Soc. 72, 14 (1950).
11. C. G. Overberger, D. Schoene, P. Kamath, and J. Taschlich, J. Org. Chem. 19, 1486 (1954).
12. E. N. Prilezhaeva, L. V. Tsymbal, O. N. Domanina, T. N. Shkurina, and M. F. Shostakovskii, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk. (1960), No. 4. *
13. R. B. Thompson, J. A. Chenicek, and T. Symon, J. Ind. Eng. Chem. 50, 797 (1958).
14. M. Karasch and C. Fuchs, J. Org. Chem. 13, 97 (1948).
15. M. F. Shostakovskii, E. N. Prilezhaeva, and N. I. Uvarova, Izvest. Akad. Nauk SSSR, Otdel Khim. Nauk (1955), p. 906.*
16. I. N. Nazarov and M. V. Kuvarzina, Izvest. Akad. Nauk SSSR, Otdel Khim. Nauk (1948), p. 599; A. A. Petrov and N. P. Sopov, Zhur. Obshch. Khim. 17, 1295 (1947).
17. Tanaka Makoto, J. Chem. Soc., Japan Industr. Chem. Soc. 60, 1509 (1957).
18. C. Djerassi, Chem. Revs. 43, 271 (1948).
19. F. Bodroux, Compt. rend. 136, 1139 (1903).
20. P. J. Boutan and F. G. Bordwell, J. Am. Chem. Soc. 79, 717 (1957).

* Original Russian pagination. See C. B. translation.

PHENTHIAZONES

IV. BROMOPHENTHIAZINESULFOXIDES AND BROMODIPHENYLAMINESULFONES

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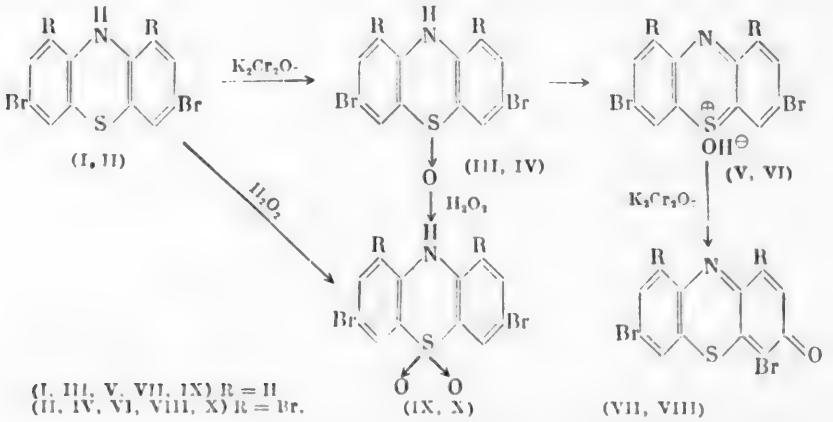
We have shown in previous work [1] that bromophenthiazines obtained in the bromination of phenthiazine are transformed by the action of potassium bichromate in boiling 100% acetic acid into bromophenthiazones. We have assumed that in this reaction the intermediate products are bromophenthiazinesulfoxides (bromophenthiazine-5-oxides) and phenazthionium hydroxide which are further rearranged into bromophenthiazones. This assumption is based on the fact that in the case of the transformation of chlorophenthiazines into chlorophenthiazones we showed experimentally the formation of chlorophenthiazinesulfoxides as intermediate reaction products [2].

To test this, we prepared bromophenthiazinesulfoxides and transformed them into bromophenthiazones. When potassium bichromate acted on 3,7-dibromophenthiazine (I) under mild conditions, we obtained 3,7-dibromophenthiazinesulfoxide (III). 1,3,7,9-Tetrabromophenthiazine (II) went over to the corresponding sulfoxide (IV) under the same conditions. At the same time occurred formation of bromophenazthionium hydroxides (V, VI) (isomers of the sulfoxides). We succeeded in isolating only the sulfoxides; separation of the bromophenazthionium hydroxides in the pure form is unlikely. On the other hand, we showed that when the bromophenthiazinesulfoxides were boiled in glacial acetic acid, the solution took on a red color like the chlorophenthiazinesulfoxides due to the establishment of an equilibrium between sulfoxides and phenazthionium hydroxides.

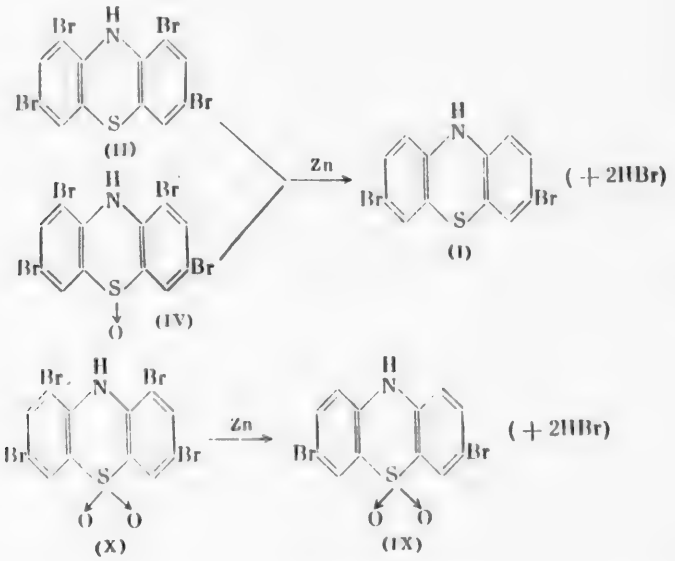
Bromophenthiazinesulfoxides and bromophenazthionium hydroxides were transformed into bromophenthiazones by the action of potassium bichromate; thus it was confirmed beyond doubt that they are intermediate products in the reaction of conversion of bromophenthiazines into bromophenthiazones (VII, VIII).

Using hydrogen peroxide as the oxidizing agent instead of bichromate, we oxidized the sulfoxides to sulfones (IX, X). The same sulfones were also obtained by oxidizing the bromophenthiazines with hydrogen peroxide.



To confirm the structure of 3,7-dibromophenthiazinesulfoxide (III) we reduced it with zinc dust in glacial acetic acid and obtained 3,7-dibromophenthiazine (I). In the reduction of 1,3,7,9-tetrabromophenthiazinesulfoxide (IV) under similar conditions we also obtained 3,7-dibromophenthiazine (I) instead of 1,3,7,9-tetrabromophenthiazine (II). This shows that the atoms of bromine substituted in positions 1,9 are sufficiently mobile and can be replaced by hydrogen atoms.

Like all sulfones, the bromodiphenylaminesulfones are not reduced to the corresponding bromophenthiazines, but the bromine atoms which occupy the 1,9 positions in 1,3,7,9-tetrabromodiphenylaminesulfone (X) are also mobile and in reduction are replaced by hydrogen. This also occurs in the case of 1,3,7,9-tetrabromophenthiazine (II).



The mobility (lability) of the bromine atoms in bromophenthiazines, bromophenthiazinesulfoxides, and bromodiphenylaminesulfones opens a new path to the preparation of other derivatives of the phenthiazine series. At the same time, we can conclude that in the unsubstituted phenthiazines positions 3,7 are more reactive than positions 1,9. Due to this, the bromine atoms which occupy positions 3,7 are more strongly bound to the phenthiazine ring and cannot be replaced by hydrogen under the conditions described above. This fact is also found in the case of unsubstituted diphenylaminesulfones.

EXPERIMENTAL

3,7-Dibromophenthiazinesulfoxide (III). Four g of (I) with an equal amount of powdered potassium bichromate was suspended in 600 ml of 80% acetic acid and the resulting mixture boiled under reflux for 15 minutes. We obtained a red solution which was filtered and poured into water. The precipitate was separated, washed well with water, and dried. The resulting substance had a rose-red color and decomposed at 240-241°. After one recrystallization from alcohol with active charcoal it formed white, glittering crystals which decomposed at 256-257°. Yield about 64%.

Difficultly soluble in benzene and toluene, easily soluble in alcohol and acetic acid.

Found %: Br 43.22; N 3.86. $C_{12}H_7ONSBr_2$. Calculated %: Br 42.90; N 3.75.

1,3,7,9-Tetrabromophenthiazinesulfoxide (IV). A mixture of 7 g of (II) with an equal amount of powdered potassium bichromate was suspended in 2.100 liters of 95% acetic acid and boiled under reflux for 35 minutes. The resulting red solution was filtered, activated charcoal was added to the filtrate and it was shaken for 5 minutes, filtered again, and the solution was poured into distilled water. The rose colored precipitate which formed was filtered, washed well with water, and recrystallized from alcohol with activated charcoal; decomposition point

235-236°. After recrystallization from dioxane with activated charcoal there were white needles with decomposition point 238-239°. Yield about 56%. Moderately soluble in acetic acid, toluene, and dioxane, soluble with difficulty in alcohol.

Found %: Br 59.99; N 2.65. $C_{12}H_5ONSBr_4$. Calculated %: Br 60.26; N 2.63.

4,7-Dibromo-3-phenthiazone (VII). Five g of (III) with an equal amount of powdered potassium bichromate was dissolved in 250 ml of 100% acetic acid with boiling, and then another 10 g of potassium bichromate was added and the solution was boiled under reflux for 15 minutes. Distilled water was added carefully to the boiling solution until slight separation of crystals stopped, and it was filtered. After it had stood for 18-20 hours, the red crystals which precipitated were filtered off, washed with water, and dried. M. p. 234-235°. After recrystallization from dioxane, glittering needles with a copper color. M. p. 239-240°. Easily soluble in acetone and benzene, moderately so in alcohol and acetic acid. Mixed melting point with (VII) obtained by the action of potassium bichromate on (I) (under the same conditions) gave no depression.

Found %: Br 42.90; N 3.70. $C_{12}H_5ONSBr_2$. Calculated %: Br 43.12; N 3.77.

1,4,7,9-Tetrabromo-3-phenthiazone (VIII). Five g of (IV) with an equal amount of powdered potassium bichromate was suspended in 500 ml of 100% acetic acid and the mixture was heated; then we added another 10 g of potassium bichromate and continued boiling under reflux for 15 minutes. Distilled water was added to the solution until there was no weak separation of crystals. After standing 4-5 hours the red needle-shaped crystals were filtered off, washed with distilled water, and dried. M. p. 257-258°. After recrystallization from toluene, red needles with m. p. 263-264°. Yield 35%. The substance was difficultly soluble in alcohol and acetic acid, easily so in acetone and toluene, and very easily so in chloro- and nitrobenzene. A mixed melting point with (VIII) obtained by the action of potassium bichromate on (II) (under the same conditions) gave no depression.

Found %: C 27.50; H 0.75; Br 60.31. $C_{12}H_3ONSBr_4$. Calculated %: C 27.22; H 0.56; Br 60.49.

3,7-Dibromodiphenylaminesulfone (IX). To 2 g of (I) in a 500 ml round bottomed flask, we added 200 ml of glacial acetic acid and heated the mixture to solution of the dibromophenthiazine. Then the resulting solution was treated with 45 ml of 30% hydrogen peroxide, added over 2 hours through the reflux condenser. The contents of the flask were poured into water, the precipitate was filtered off and recrystallized from acetic acid with activated charcoal. White crystals with m. p. 340-341°. Yield 63%.

Found %: Br 41.42; N 3.59. $C_{12}H_7O_2NSBr_2$. Calculated %: Br 41.13; N 3.59.

The same treatment, starting from (III), gave (IX).

1,3,7,9-Tetrabromodiphenylaminesulfone (X). To 2 g of (II) in a 500 ml round-bottomed flask was added 300 ml of glacial acetic acid. The resulting suspension was treated as described above with 50 ml of hydrogen peroxide. After some time, the suspension dissolved completely. At the end of the reaction, the contents of the flask were poured into water, the precipitate was filtered off, washed with water, and dried. After recrystallization from toluene, white crystals with m. p. 252-253°. Yield 75%.

Found %: Br 58.23; N 2.81. $C_{12}H_5O_2NSBr_4$. Calculated %: Br 58.50; N 2.55.

The same treatment, starting from substance (IV) gave (X).

Reduction of substance (III) to (I). Two g of (III) was boiled for half an hour with zinc dust in 200 ml of acetic acid. The residue of zinc was removed by filtration and the filtrate was poured into water. The precipitate was filtered off, washed with water, and crystallized from acetic acid, decomposition point 210-211°. A mixed sample with (I) gave no depression in melting point. Yield about 70%.

Reduction of substance (IV) to (I). Two g of (IV) was reduced with zinc dust by boiling for four hours in glacial acetic acid. Treatment was as in the preceding experiment and yielded silvery plates with decomposition point 210-211°. A mixed sample with (I) gave no depression of melting point. Yield 66%.

Found %: C 40.51; H 2.10; N 4.01. $C_{12}H_7NSBr_2$. Calculated %: C 40.33; H 1.96; N 3.92.

Reduction of substance (X) to (IX) occurred under the same conditions as in the previous experiment, but with three hour boiling. We obtained crystals with m. p. 340-341°. A mixed melting point with (IX) obtained by oxidation of (I) with hydrogen peroxide gave no depression. Yield 71%.

Found %: Br 41.30; N 3.62. $C_{12}H_7O_2NSBr_2$. Calculated %: Br 41.13; N 3.59.

Reduction of substance (II) to (I). Two g of (II) was suspended in 500 ml of glacial acetic acid and boiled for five hours; zinc dust was added in small portions each half hour. The suspension gradually dissolved. After removal of the zinc residue, the solution was poured into water. The precipitate was filtered off, washed with water, and crystallized from acetic acid; decomposition point 210-211°. A mixed sample with (I) obtained from bromination of phenthiazine gave no depression of melting point. Yield 64%.

SUMMARY

1. We have prepared bromophenthiazinesulfoxides which are converted by potassium bichromate into bromothiazones. We have shown that the bromophenthiazinesulfoxides are intermediate products in the reaction of conversion of bromophenthiazines into bromophenthiazones.

2. When bromophenthiazinesulfoxides are oxidized by hydrogen peroxide, they give the corresponding sulfones.

3. Bromine atoms substituted in the 1,9 positions in 1,3,7,9-tetrabromophenthiazine, -bromophenthiazine-sulfoxide and bromodiphenylaminesulfone are quite mobile and are replaced by hydrogen during reduction.

LITERATURE CITED

1. C. Bodea and M. Raileanu, Lieb. Ann (1959).
2. C. Bodea and M. Raileanu, Lieb. Ann 614, 171 (1958).

THE ACYLATION OF AMINO ACIDS AND PEPTIDES BY 2-METHYLCYCLOPENTANONE-3-CARBOXYLIC ACID

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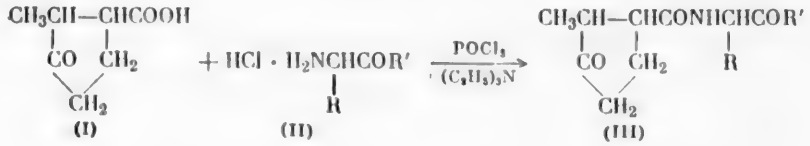
At the present time there is often a need to acylate peptides by various acids in order to obtain biologically active compounds (sarcolysylpeptides, actinomycin, etc. [1]). For preparing such compounds, we thought it would be interesting to use, besides the ordinary acylation methods, special methods used for creating peptide bonds. However, it was shown that many methods which succeed in creating peptide bonds cannot be used for introduction of acyl residues in the molecule of amino acids and peptides. Thus, in the acylation by 2-methylcyclopentanone-3-carboxylic acid (dihydrosarcomycin) (I) of the esters of some amino acids, and also of di- and tripeptides with acid chlorides [2], and with the dicyclohexylcarbodiimide method [3] or the method of activated esters [4], we obtained only negative results. Only the use of the method of mixed anhydrides ($POCl_3$) [5] permitted us to obtain the corresponding acylated derivatives of amino acids and peptides (III) in the crystalline state.



The name of the radicals in compounds of types (II) and (III) are given in Table 1.

In order to obtain the starting esters of dipeptides (IIb) - (IId) we carried out the synthesis of esters of the corresponding N-carbobenzoxypeptides by the method of activated esters [6] followed by removal of the carbobenzoxy group. For synthesis of the tripeptides (IIe) and (IIf) the esters of peptides (IIb) and (IId) were saponified [7] to the corresponding acids and then condensed with the ethyl ester of D,L-phenylalanine in the presence of N,N'-dicyclohexylcarbodiimide [8]. The subsequent removal of the carbobenzoxy group was carried out in all cases by hydrogenation [9]. The resulting hydrochlorides of the ethyl esters of type (II) di- and tripeptides were acylated by dihydrosarcomycin without further purification, using phosphorus oxychloride in the presence of triethylamine [5]. The characteristics of the resulting compounds of type (III) are given in Table 2.

EXPERIMENTAL

Obtaining cyanomethyl esters of N-carbobenzoxyamino acids and dihydrosarcomycin. The synthesis of cyanomethyl esters of N-carbobenzoxy-D,L-leucine (m. p. 83-85°, from ether) [10], N-carbobenzoxyglycine (m. p. 69-70°, from ether) [11], N-carbobenzoxy-D,L-valine, and dihydrosarcomycin was carried out by the method of Schwyzer [4, 10, 11].

TABLE 1

Type of compound	R	R'
IIa IIIa	H	OC_2H_5
IIb IIIb	H	$NHCHCOOC_2H_5$ CH_3
IIc IIIc	$(CH_3)_2CH$	$NHCH_2COOC_2H_5$
IId IIId	$(CH_3)_2CHCH_2$	$NHCH_2COOC_2H_5$
IIe IIIe	H	$NHCHCONHCHCOOC_2H_5$ CH_3 $CH_2C_6H_5$
IIf IIIf	$(CH_3)_2CHCH_2$	$NHCH_2CONHCHCOOC_2H_5$ $CH_2C_6H_5$
IIIg	$(CH_3)_2CH$	$NHCH_2COOH$
IIIh	$(CH_3)_2CHCH_2$	$NHCH_2COOH$

The cyanomethyl ester of N-carbobenzoxy-D,L-valine was obtained with a yield of 72%, m. p. 82-83° (from absolute ether).

Found %: C 61.71; H 5.78; N 9.69. $C_{15}H_{18}O_4N_2$. Calculated %: C 62.04; H 6.25; N 9.65.

The cyanomethyl ester of dihydrosarcomycin was obtained with a yield of 62%. B. p. 115-117° (1 mm), $n^{18}D$ 1.4710.

Found %: C 59.62; H 6.39; N 7.83. $C_9H_{11}O_3N$. Calculated %: C 59.63; H 6.12; N 7.74.

Obtaining the ethyl esters of N-carbobenzoxydipeptides. The condensation of the cyanomethyl esters of the carbobenzoxyamino acids with the corresponding ethyl esters of glycine and alanine was carried out under the conditions described by Schwyzer [6]. By this method we prepared the ethyl esters of N-carbobenzoxy-D,L-valylglycine with a 60% yield (m. p. 144-145°, from alcohol) [12], of N-carbobenzoxy-D,L-leucylglycine with a yield of 70% (m. p. 85-86°, from acetone-ether) [10], and of N-carbobenzoxyglycyl-D,L-alanine (oil, yield quantitative).

Obtaining N-carbobenzoxydipeptides. The ethyl esters of N-carbobenzoxy-D,L-leucylglycine and N-carbobenzoxyglycyl-D,L-alanine were saponified in methyl alcohol with 2 N NaOH at 18-23° for 20 minutes [7]. After acidification, we obtained N-carbobenzoxy-D,L-leucylglycine in 96% yield (m. p. 162-163°, from methyl alcohol) [10], and N-carbobenzoxyglycyl-D,L-alanine in yield of 83% (m. p. 175-176°, from methyl alcohol) [13].

Obtaining ethyl esters of N-carbobenzoxytripeptides. To a suspension of 0.0075 mole of N-carbobenzoxydipeptide in 10 ml of methylene chloride was added a solution of 0.015 mole of ethyl ester of D,L-phenylalanine in 10 ml of acetonitrile, and the clear solution was treated with 0.0075 mole of N,N'-dicyclohexylcarbodiimide [8] in 5 ml of methylene chloride. The mixture was allowed to stand at 18-23° for 45 hours. The precipitate of N,N'-dicyclohexylurea was filtered off and the filtrate was evaporated dry. The residue was extracted with ethyl acetate which was washed with 1 N HCl, 1 N $NaHCO_3$, and water and dried over Na_2SO_4. After distillation of the solvent in a vacuum, the ethyl esters of the N-carbobenzoxytripeptides were obtained in the form of oils which solidified after grinding with anhydrous ether. We thus synthesized the ethyl ester of N-carbobenzoxyglycyl-D,L-alanyl-D,L-phenylalanine with a yield of 85% and of N-carbobenzoxy-D,L-leucylglycyl-D,L-phenylalanine with a yield of 72%. These compounds were reduced without further purification.

TABLE 2

Compd. Nos.	Name	M.p.	Solvent for recrystallization	Yield %	Found, %			Empirical formula	Calculated, %		
					C	H	N		C	H	N
IIIa	Ethyl dihydrosarcomycylglycinate	86—87°	Anhydrous alcohol and absolute ether (1 : 10)	30	58.39	7.62	6.41	$C_{11}H_{17}O_4N$	58.13	7.54	6.16
IIIb	Ethyl dihydrosarcomycylglycylalaninate	142—143	Absolute ether	18	56.15	7.34	9.40	$C_{14}H_{22}O_5N_2$	56.36	7.43	9.39
IIIc	Ethyl dihydrosarcomycylvalylglycinate	183—184	Anhydrous alcohol	30	58.72	8.14	8.74	$C_{16}H_{26}O_5N_2$	58.88	8.03	8.58
IIId	Ethyl dihydrosarcomycylleucylglycinate	120—121	Alcohol	31	60.10	8.38	8.53	$C_{17}H_{28}O_5N_2$	59.98	8.29	8.23
IIIe	Ethyl dihydrosarcomycylglycylalanylphenylalaninate	133—135	Anhydrous alcohol	20	62.29	6.65	9.52	$C_{23}H_{31}O_6N_3$	62.01	6.98	9.43
IIIf	Ethyl dihydrosarcomycylleucylglycylphenylalaninate	176—178	Anhydrous alcohol	16	63.60	7.69	8.89	$C_{26}H_{37}O_6N_3$	63.84	7.65	8.61
IIIg	Dihydrosarcomycylvalylglycine	206—208	Water	21	56.45	7.44	9.51	$C_{14}H_{22}O_5N_2$	56.36	7.43	9.39
IIIh	Dihydrosarcomycylleucylglycine	147—148	Anhydrous alcohol	17	58.00	8.03	8.67	$C_{15}H_{24}O_5N_2$	57.69	7.74	8.96

Obtaining the hydrochlorides of ethyl esters of di- and tripeptides of type (II). To a solution of 0.005 mole of ethyl ester of N-carbobenzoxydi- or tripeptides in 15-20 ml of methyl alcohol we added 0.005 mole of a titrated alcoholic solution of HCl and 1 g of 10% palladium on carbon. Hydrogenation was carried out at normal pressure and 18-23° for 2.5-4 hours. At the end of hydrogen absorption the catalyst was filtered off and washed with methyl alcohol, and the filtrate was evaporated in a vacuum at 25-30°. The hydrochlorides of the ethyl esters of di- and tripeptides, obtained as glassy masses, were dried in a vacuum over P_2O_5 and without purification were used for further transformations. Thus, we obtained in quantitative yields the hydrochlorides of the ethyl esters of the following peptides: glycyl-D,L-alanine (IIb), D,L-valylglycine (IIc), D,L-leucylglycine (IId), glycyl-D,L-alanyl-D,L-phenylalanine (IIe), and D,L-leucylglycyl-D,L-phenylalanine (IIf).

Condensation of dihydrosarcomycin with the hydrochlorides of the ethyl esters of amino acids, and also of di- and tripeptides. To a solution of 0.01 mole of dihydrosarcomycin in 15 ml of methylene chloride we added a solution of 0.01 mole of the hydrochloride of the ethyl ester of one of the compounds of type (II) in 20 ml of methylene chloride which contained 0.01 mole of triethylamine. The mixture was cooled to − 15° and in the course of one minute, with energetic stirring, we added a suspension of 0.01 mole of $POCl_3$ and 0.02 mole of triethylamine in 10 ml of methylene chloride. After stirring at − 15° for one hour, we added to the reaction mixture 20 ml of water, and then the methylene chloride was distilled off in a vacuum. The residue was extracted with ethyl acetate and the solution was washed with 5% $NaHCO_3$ and water. After drying and distillation of the solvent, we obtained compounds of type (III), which were recrystallized from the corresponding solvents. Alkaline saponification of the ester group [7] from compounds (IIIc) and (IIId) gave the corresponding acids (IIIg) and (IIIh). The properties and yields of the resulting compounds of type (III) are given in Table 2.

SUMMARY

Using the method of mixed anhydrides with phosphorus oxychloride we have carried out the acylation of esters of amino acids, and also of di- and tripeptides, with 2-methylcyclopentanone-3-carboxylic acid (dihydrosarcomycin).

LITERATURE CITED

1. I. L. Knunyants, O. V. Kil'disheva, and N. E. Golubeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, (1956), p. 1418;* N. E. Golubeva, O. V. Kil'disheva, and I. L. Knunyants, Doklady Akad. Nauk SSSR 119, 83 (1958);* A. S. Khokhlov and M. M. Shemyakin, Khim. Nauka i Prom. 1, 377 (1956); L. F. Larionov, Khim. Nauka i Prom. 1, 441 (1956); A. S. Khokhlov and N. M. Vikhrova, Antibiotiki 3, 1-36 (1958); J. C. Sheehan, H. G. Zachan, and W. B. Lawson, J. Am. Chem. Soc. 79, 3933 (1957); 80, 3349 (1958); W. Keller-Schierlein, M. L. Mihailovic, and V. Prelog, Helv. Chim. Acta 42, 305 (1959).
2. T. Wieland, Ang. Chem. 63, 7 (1951).
3. J. C. Sheehan and G. P. Hess, J. Am. Chem. Soc. 77, 1067 (1955).
4. R. Schwyzer, B. Iselin, and M. Feurer, Helv. Chim. Acta 38, 69 (1955).
5. T. Wieland and B. Heinke, Lieb. Ann. 599, 70 (1956).
6. R. Schwyzer, M. Feurer, and B. Iselin, Helv. Chim. Acta 38, 83 (1955).
7. M. Bergmann, L. Zervas, and J. Fruton, J. Biol. Chem. 111, 226 (1935).
8. S. Shankman and Y. Schvo, J. Am. Chem. Soc. 80, 1164 (1958).
9. B. Iselin, M. Feurer, and R. Schwyzer, Helv. Chim. Acta 38, 1508 (1955).
10. R. Schwyzer and B. Iselin, Biochem. of Nitrogen, Helsinki, 181 (1955).
11. R. Schwyzer, M. Feurer, B. Iselin, and H. Kägi, Helv. Chim. Acta 38, 80 (1955).
12. R. Kuhn and H. W. Ruelius, Ber. 85, 38 (1952).
13. T. Wieland and R. Schring, Lieb. Ann. 569, 122 (1950).

* Original Russian pagination. See C. B. translation.

A NEW METHOD FOR SYNTHESIS OF O-PEPTIDES

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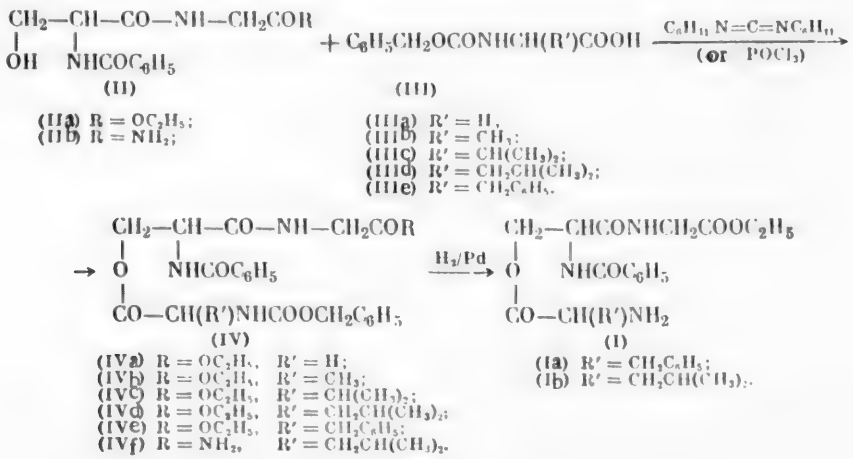
A study of the properties of O-peptides of β-hydroxy-α-amino acids is of great interest in connection with the possible biochemical importance of these compounds [1, 2], which is suggested by the recent work of Brenner on aminoacyl uptake [3]. However, the preparation of O-peptides is in many cases a complex problem and this apparently explains the comparatively small number of compounds of this type described in the literature. Among the many different methods known at present for creating peptide bonds, only two are used for the synthesis of O-peptides, namely: the acid chloride method [4-7] and the method of mixed anhydrides [1, 7, 8].

In studying the properties of O-peptides, we encountered the problem of obtaining a number of previously undescribed O-peptides of the N-benzoylserine type (I). We found difficulties in preparing such compounds. One of the paths which we tried consisted in the action on the ethyl ester of N-benzoylserylglycine of the N-carboxyanhydride of amino acids in the presence of hydrogen chloride (see [1]). However, this method did not give the desired results. Another path chosen by us for the synthesis of compounds of type (I) was the acylation of the hydroxy groups of N-benzoylserine by acid chlorides [6] or mixed anhydrides ($COCl_2$) of carbobenzoxy-amino acids [8] with later condensation of the resulting O-peptide with amino acid esters and with splitting off of the protective carbobenzoxy group. However, this method also failed to permit isolation of O-peptides of type (IV, I) in the individual state.

These negative results compelled us to search for different processes for getting O-peptide bonds. In the studies which we carried out we found two new methods for the synthesis of O-peptides. In one of these methods, the creation of an O-peptide bond occurred by condensation of the ethyl ester of N-benzoylserylglycine (IIa) with N-carbobenzoxy amino acids (III) with the aid of N,N'-dicyclohexylcarbodiimide (see [9-11]), in the other, with the aid of phosphorus oxychloride [14].



(II)

(IIa) R = OC_2H_5;
(IIb) R = NH_2;

(III)

(IIIa) R′ = H;
(IIIb) R′ = CH_3;
(IIIc) R′ = $CH(CH_3)_2$;
(IIId) R′ = $CH_2CH(CH_3)_2$;
(IIIe) R′ = $CH_2C_6H_5$.

(IV)

(IVa) R = OC_2H_5, R′ = H;
(IVb) R = OC_2H_5, R′ = CH_3;
(IVc) R = OC_2H_5, R′ = $CH(CH_3)_2$;
(IVd) R = OC_2H_5, R′ = $CH_2CH(CH_3)_2$;
(IVe) R = OC_2H_5, R′ = $CH_2C_6H_5$;
(IVf) R = NH_2, R′ = $CH_2CH(CH_3)_2$.

(I)

(Ia) R′ = $CH_2C_6H_5$;
(Ib) R′ = $CH_2CH(CH_3)_2$.

In obtaining compounds of type (IV) by the carbodiimide method, the starting reagents were taken in equimolar ratio. The process was carried out at room temperature for 24 hours in a medium of acetone or dimethylformamide in the presence of pyridine. The precipitate of N,N'-dicyclohexylurea was filtered off and the O-peptides of type (IV) were obtained from the filtrate in the crystalline state with a good yield. By this method, we obtained the ethyl esters of O-carbobenzoxyaminoacyl-N-benzoylserylglycines (IVa-IVe). Under analogous conditions, we obtained from the amide of N-benzoylserylglycine (IIb) and carbobenzoxyleucine (IIId) the amide of O-carbobenzoxyleucyl-N-benzoylserylglycine (IVf). Also, in the case of synthesis of the ethyl ester of O-carbobenzoxyleucyl-N-acetyltyrosine (V) and the amide of O-carbobenzoxyphenylalanylsalicylic acid (VI) we showed that the carbodiimide method for the synthesis of O-peptide bonds which we have suggested can be used successfully for aminoacylation of phenolic hydroxyl groups. This method is characterized by experimental simplicity and good yields of the resulting O-peptides (see table).

In the synthesis of O-peptides of type (IV) by the method of mixed anhydrides using phosphorus oxychloride, the reagents were taken in equimolar amounts; the process was carried out at $-15°$ in a medium of dry methylene chloride in the presence of triethylamine. By this process, we obtained in the crystalline state the compounds (IVb) to (IVe), but the yield of O-peptides by this method was considerably lower than by the carbodiimide method.

In several of the O-peptides of type (IV), catalytic hydrogenation under the usual conditions [12] removed the protective carbobenzoxy group and gave the corresponding O-peptides with free amino groups (Ia), (Ib). Thus, the use of N,N'-dicyclohexylcarbodiimide and phosphorus oxychloride for creating O-peptide bonds permits us to synthesize a series of such O-peptides of serine which cannot be obtained in the crystalline state by the methods described in the literature.

EXPERIMENTAL

1. Ethyl ester of N-benzoylserylglycine (IIa). To a suspension of 10.4 g (0.05 mole) of N-benzoylserine [13] in 45 ml of methylene chloride was added 7.7 g (0.07 mole) of ethyl glycinate in 10 ml of methylene chloride. To the resulting solution was added 10.3 g (0.05 mole) of N,N'-dicyclohexylcarbodiimide dissolved in 25 ml of methylene chloride. After several minutes a precipitation of N,N'-dicyclohexylurea began, accompanied by some heating of the reaction mixture. After 24 hours, the N,N'-dicyclohexylurea was filtered off. The filtrate was washed successively with 1 N HCl, 1 N $NaHCO_3$, and water, and dried over Na_2SO_4; it was evaporated in a vacuum at 30°, and gave 8 g (54 %) of ester (IIa), m. p. 119-120° (from anhydrous alcohol).

Found %: C 57.11; H 6.24; N 9.54. $C_{14}H_{16}O_5N_2$. Calculated %: C 57.13; H 6.17; N 9.52.

2. Amide of N-benzoylserylglycine (IIb). We dissolved 3.5 g (0.012 mole) of ethyl ester of N-benzoylserylglycine (IIa) in 100 ml of anhydrous alcohol. We passed into the solution for 4 hours at 0° a stream of dry ammonia, and allowed the mixture to stand at room temperature for 72 hours. Then the solvent was distilled off in a vacuum and we obtained amide (IIb). Weight 2.5 g (80%), m. p. 139-140° (alcohol and ethyl acetate, 1:1).

Found %: C 54.26; H 5.86; N 15.75. $C_{12}H_{15}O_4N_3$. Calculated %: C 54.34; H 5.70; N 15.84.

3. Obtaining O-peptides of type (IV). a) Using N,N'-dicyclohexylcarbodiimide. To a solution of equimolar amounts of the acylating component of type (II) and N-carbobenzoxyamino acid (III) in a minimal amount of acetone* we added an equimolar amount of pyridine and then an equimolar amount of N,N'-dicyclohexylcarbodiimide dissolved in the minimal amount of acetone. The reaction mixture remained for 24 hours at room temperature, and then the precipitated N,N'-dicyclohexylurea was filtered off and washed with a small amount of acetone. The filtrate was evaporated dry in a vacuum and the oily residue was dried in a vacuum desiccator and ground with a mixture of ethyl acetate and ligroin to the formation of a crystalline substance

* In all the experiments which we ran the solvent was acetone, and only in the case of the amide of N-benzoylserylglycine did we use dimethylformamide as the solvent.

Compd. Nos.	Name of O-peptide	M.p. (solvent)	Found, %			Empirical formula	Calculated, %			Yield, %	
			C	H	N		C	H	N	meth. 3a	meth. 3b
(IVa)	Ethyl ester of O-cbz*-glycyl-N-benzoylserylglycine	127-129° (aqueous C_2H_5OH)	59.62	5.69	8.69	$C_{24}H_{27}O_8N_3$	59.36	5.60	8.65	64	—
(IVb)	Ethyl ester of O-cbz-alanyl-N-benzoylserylglycine	130-131° (ethyl acetate-ligroin)	60.36	5.96	8.41	$C_{25}H_{29}O_8N_3$	60.10	5.84	8.40	68	30
(IVc)	Ethyl ester of O-cbz-valyl-N-benzoylserylglycine	148-149° (ethyl acetate)	61.41	6.43	7.87	$C_{27}H_{33}O_8N_3$	61.47	6.31	7.96	67	20
(IVd)	Ethyl ester of O-cbz-leucyl-N- benzoylserylglycine	118-120° (C_2H_5OH)	62.27	6.66	7.81	$C_{28}H_{35}O_8N_3$	62.09	6.51	7.75	84	40
(IVe)	Ethyl ester of O-cbz-phenylalanyl-N-benzoylserylglycine	149-152° (C_2H_5OH)	65.06	6.10	7.33	$C_{31}H_{33}O_8N_3$	64.68	5.78	7.29	82	40
(IVf)	Amide of O-cbz-leucyl-N-benzoylserylglycine	132-134° (ethyl acetate)	60.77	6.43	11.14	$C_{26}H_{32}O_7N_4$	60.93	6.28	10.92	69	—
(V)	Ethyl ester of O-cbz-leucyl-N-acetyltyrosine	126-128° (aqueous CH_3OH)	64.98	6.96	5.48	$C_{27}H_{34}O_7N_2$	65.05	6.94	5.61	75	—
(VI)	Amide of O-cbz-phenylalanylsalicylic acid	170-172° (aqueous C_2H_5OH)	69.01	5.36	6.77	$C_{24}H_{22}O_5N_2$	68.90	5.30	6.69	85	—

* cbz=carbobenzoxy

which was filtered off and recrystallized from the respective solvent. The characteristics of the compounds (IVa) - (IVf), (V), and (VI) are given in the table.

b) Using phosphorus oxychloride. Equimolar amounts (of 0.005 mole) of the ethyl ester of N-benzoylserylglycine (IIa), N-carbobenzoxyamino acids (IIIb) - (IIIe) and triethylamine were dissolved in 35 ml of methylene chloride. The solution was cooled to − 15° and kept at a temperature of − 12 to − 10°; with stirring we added a suspension obtained by mixing 0.01 mole of triethylamine and 0.005 mole of phosphorus oxychloride in 2 ml of methylene chloride. The stirring was continued at − 12 to − 10° for another hour and then the reaction mixture was gradually treated with 10 ml of water. The methylene chloride layer was separated, washed with a cold 5% solution of soda, with water, and dried over Na_2SO_4. The methylene chloride was distilled off in a vacuum, the oily residue was dissolved in hot ethyl acetate, and was precipitated by ligroin (1 : 10); it was separated, dried in a vacuum desiccator, and recrystallized from the respective solvent. The characteristics of the resulting O-peptides of type (IV) are given in the table.

4. Obtaining the O-peptides of type (I). We dissolved 1.4 g (0.0025 mole) of the ethyl ester of O-carbobenzoxyphenylalanyl-N-benzoylserylglycine (IVe) in 40 ml of methyl alcohol, added 0.6 g of 10% Pd on carbon and an equimolar amount of alcoholic HCl solution, and hydrogenated at room temperature and atmospheric pressure. Then the catalyst was filtered off and the solution was evaporated in a vacuum. The resulting oily hydrochloride of the ethyl ester of O-phenylalanyl-N-benzoylserylglycine (Ia) after drying in a vacuum desiccator changed into a white, amorphous powder. Weight 1.1 g (98%).

Found %: N 8.70. $C_{23}H_{23}O_6N_3Cl$. Calculated %: N 8.79.

Under analogous conditions, we carried out the hydrogenation of the ethyl ester of O-carbobenzoxyleucyl-N-benzoylserylglycine (IVd). The yield of hydrochloride of the ethyl ester of O-leucyl-N-benzoylserylglycine (Ib) was 99%.

Found %: N 9.16. $C_{20}H_{30}O_6N_3Cl$. Calculated %: N 9.47.

SUMMARY

We have shown that two known methods for the synthesis of peptide bonds (the carbodiimide method and the method of mixed anhydrides with phosphorus oxychloride) can be used successfully for the synthesis of O-peptides.

LITERATURE CITED

1. J. A. Moore, J. R. Dice, E. D. Nicolaides, R. D. Westland, and E. L. Wittle, J. Am. Chem. Soc. 76, 2884 (1954); E. D. Nicolaides, R. D. Westland, and E. L. Wittle, J. Am. Chem. Soc. 76, 2887 (1954).
2. M. M. Botvinnik and S. M. Avaeva, Doklady Akad. Nauk SSSR 84, 951 (1952); M. M. Botvinnik, S. M. Avaeva, M. I. Konovalova, and V. I. Ostoslavskii, Zhur. Obshch. Khim. 27, 1910 (1957);* M. M. Botvinnik and S. M. Avaeva, Doklady Akad. Nauk SSSR 112, 1053 (1957).*
3. M. Brenner, J. P. Zimmermann, J. Wehrmüller, and P. Quitt, J. Photaki Experientia 11, 397 (1955); M. Brenner, J. P. Zimmermann, J. Wehrmüller, P. Quitt, A. Hartmann, W. Schneider, and U. Beglinger, Helv. Chim. Acta 40, 1497 (1957); M. Brenner, Ang. Chem. 21, 677 (1957); 70, 80 (1958).
4. E. Abderhalden and E. Bahn, Z. Physiol. Chem. 234, 181 (1935).
5. S. Kaufman and H. Neurath, Arch. Biochem. 21, 437 (1949).
6. M. M. Botvinnik, S. M. Avaeva, and E. A. Mistryukov, Zhur. Obshch. Khim. 23, 971 (1953);* M. M. Botvinnik and S. M. Avaeva, Zhur. Obshch. Khim. 26, 2329 (1956).*

* Original Russian pagination. See C. B. translation.

7. L. Velluz, G. Amiard, and R. Heymes, Bull. Soc. Chim. (1955), p. 1283.
8. M. Brenner, J. P. Zimmermann, P. Quitt, W. Schneider, and A. Hartmann, Helv. Chim. Acta 40, 604 (1957).
9. English patent 691,808 (1953).
10. G. Schulz and K. Fiedler, Ber. 89, 2681 (1956).
11. D. F. Elliott and D. W. Russell, Biochem. J. 66, 49P (1957).
12. B. Iselin, M. Feurer and R. Schwyzer, Helv. Chim. Acta 38, 1508 (1955).
13. S. P. L. Sörensen and A. C. Andersen, Z. Physiol. Chem. 56, 250 (1908).
14. T. Wieland and B. Heinke, Lieb. Ann. 599, 70 (1956).

SOME PROPERTIES OF N-BENZYLATED PEPTIDES. III

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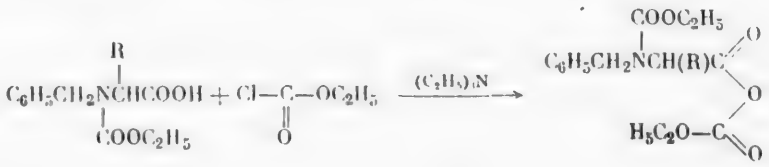
At the present time peptide synthesis occupies one of the chief places in the synthetic chemistry of proteins. In spite of great progress, there are still a number of difficulties and unsolved problems in this field. The present work is a continuation of studies in the field of the synthesis of benzylpeptides. Until now, we have succeeded in carrying out only the synthesis of benzyldi- and tripeptides, which were obtained by benzylamination of the corresponding α-halogen acylated amino acids [1] and dipeptides [2]. However, the synthesis of higher benzylpeptides by this method is difficult and this apparently explains the absence of data in the literature on their synthesis. Therefore, there is certainly interest in working out a new method for the synthesis of benzylpolypeptides. For a solution of this problem we decided to study the behavior of the benzyl derivatives of amino acids and peptides in the peptide synthesis by the method of mixed anhydrides. Although this method was suggested relatively recently, it is now rightly considered the leading one and gives the best results. It is most often used in the peptide synthesis of carbobenzoxyamino acids and peptides. Among the derivatives protected by benzyl groups, the synthesis by the method of mixed anhydrides has been applied only to dibenzylamino acids. There are no data in the literature on the application of benzylamino acids and peptides in the peptide synthesis by the method of mixed anhydrides.

We carried out the study of this problem on the following benzylamino acids and peptides: benzylphenylalanine, -leucine, -valine, and -glycylalanylphenylalanine. It was assumed that the benzylamino acids could be combined with amino acid esters by the intermediate formation of mixed anhydrides with chlorocarbonic ester. For this purpose, we combined benzylphenylalanine under these conditions with a leucine ester. As a result of study of the reaction products, carried out many times, we isolated benzylphenylalanine to the extent of 50% of that used for the reaction. Along with this, we established the formation of a new substance which differed strongly in solubility from the starting material and which therefore could easily be separated from it. By chromatography, we observed only phenylalanine in the hydrolyzate from this substance which showed its identity with the starting material, and the absence of leucine in it indicated that a combination reaction did not occur in this case. Thus, we isolated a substance which consisted of only one amino acid, phenylalanine, but which, in distinction from the original benzylphenylalanine, was easily soluble in all organic solvents. Only one structure could be assigned to this compound, namely benzyl carbethoxyphenylalanine. This compound could be considered the result of direct acylation of benzylphenylalanine by chlorocarbonic ester, which in turn indicates the characteristic behavior of the hydrogen on the nitrogen in the structure of benzylphenylalanine.

In order to confirm this, we carried out a study of the products from the reaction of chlorocarbonic ester with benzylamino acids under conditions for formation of a mixed anhydride, but without addition of the second component. In all cases, we isolated benzyl carbethoxyamino acids from the reaction, and this, in distinction from the benzylamino acids, was an oil which was easily soluble in organic solvents. The homogeneity of this substance was confirmed by ionophoretic experiments which showed the electrical neutrality of the resulting compound in 30% acetic acid, in distinction from the electropositivity of the starting benzylamino acid. Since these compounds were obtained by us for the first time and we could not crystallize them, we identified them by comparison with the benzyl carbethoxyamino acids obtained from benzylamino acids and chlorocarbonic ester by the method of Fisher (the action of chlorocarbonic ester was carried out in an aqueous alkali medium). The

benzyl carbethoxyamino acids synthesized in this way were identical in their properties with the benzyl carbethoxyamino acids obtained earlier under conditions of mixed anhydrides.

It seemed to us no less interesting to explain the possibility of further reaction of the benzyl carbethoxyamino acids with chlorocarbonic ester with formation of mixed anhydrides. We showed that such formation of mixed anhydrides actually occurs.



We did not judge the obtaining of the anhydride by isolating it (the literature contains evidence of the instability of mixed anhydrides of acylamino acids with chlorocarbonic ester), but by the formation of peptide bonds. Thus, in the reaction of the mixed anhydride of benzyl carbethoxyvaline with the ethyl ester of glycylglycine in chloroform in the presence of a tertiary base we obtained the ethyl ester of benzyl carbethoxyvalylglycylglycine. The amino acid composition of the resulting compound (valine and glycine), its analysis, homogeneity (paper ionophoresis) and the data of spectrophotometry of its copper biuret complex left no doubt of its tripeptide structure. Thus, our preparation of benzyl carbethoxyvalylglycylglycine indicates the possibility of using benzyl carbethoxyamino acids in the peptide synthesis (by the method of mixed anhydrides).

EXPERIMENTAL

Synthesis of benzylamino acids and their derivatives. 1. Benzylphenylalanine. To a solution of 30 g of bromohydrocinnamic acid in 250 ml of absolute ether was added 55 g of benzylamine with cooling. The reaction mixture was kept for four days at room temperature. The colorless precipitate was filtered off and washed with ether. For recrystallization the substance was dissolved in 1 N NaOH and precipitated with acetic acid. A second recrystallization was carried out from nitrobenzene or glycol; the precipitate was washed with acetone. Yield 20 g (63%). M. p. 226.5° (decomposition). According to [3], m. p. 225°.

Found %: C 75.34, 75.48; H 7.16, 7.01; N 5.27, 5.07. $C_{16}H_{17}O_2N$. Calculated %: C 75.28; H 6.71; N 5.22.

2. Benzylvaline was obtained in an analogous way. Yield 51%. M. p. 235°. Not described in the literature.

Found %: N 7.01, 7.03. $C_{12}H_{17}O_2N$. Calculated %: N 6.75.

3. Benzylleucine. Yield 52%. M. p. 223°. According to [4], m. p. 225°.

Found %: N 6.83, 6.65. $C_{13}H_{19}O_2N$. Calculated %: N 6.33.

4. Benzyl carbethoxyphenylalanine. We dissolved 0.5 g of benzylphenylalanine in 5 ml of 1 N NaOH. With cooling and stirring with a mechanical stirrer we added 0.19 ml of chlorocarbonic ester. The mixture was kept for one hour with cooling and stirring, and then was acidified with hydrochloric acid to an acid reaction. The resulting precipitate, which was unreacted benzylphenylalanine (0.1 g), was separated from the solution which was repeatedly extracted with ether. The ether solution, dried over sodium sulfate, was concentrated in a vacuum. The residual oil was passed over a chromatogram (conditions for all experiments: 5 hours, buffer of 30% CH_3COOH, potential gradient 6.8 v/cm), developed to a yellow color with benzidine, and was found at the point of deposition.

Found %: N 4.28, 4.36. $C_{14}H_{21}O_4N$. Calculated %: N 4.10.

Titration according to Willstatter. A 0.2010 g sample was dissolved in 10 ml of 96% C_2H_5OH. Titration was carried out with 0.1 N alcoholic NaOH in the presence of thymolphthalein. In the titration we used 0.022 mg of alkali, with 0.025 mg calculated on benzyl carbethoxyphenylalanine.

5. Benzyl carbethoxyvaline. To a suspension of 2 g of benzylvaline in 40 ml of anhydrous chloroform was added 1.4 ml of anhydrous triethylamine. Then with cooling and stirring 0.95 ml of chlorocarbonic ester was added. The mixture remained 30 minutes in the cold and then overnight at room temperature. The precipitate (unreacted benzylvaline) was filtered off. The weight of precipitate was 0.4 g, that is, the acylation reaction took place to the extent of 80%. The chloroform filtrate was treated twice with 2 N hydrochloric acid and twice with water, and was dried over sodium sulfate. After distillation of the chloroform in a vacuum a thick yellow oil remained. When placed on an electrochromatogram (4 hours) and developed with benzidine, it gave one spot at the point of deposition.

Found %: N 5.28, 5.32. $C_{15}H_{21}O_4N$. Calculated %: N 5.01.

Saponification of benzyl carbethoxyvaline and isolation of benzyl carboxyvaline. To the preparation of benzyl carbethoxyvaline was added 40 ml of 1 N NaOH and the mixture was heated for 22 hours on a water bath. After acidification with 1 N hydrochloric acid an oil precipitated which gradually crystallized from water. After drying in a vacuum desiccator over sulfuric acid, the substance had a m. p. of 88-92°. It was developed by benzidine.

Found %: N 5.77, 5.81. $C_{13}H_{17}O_4N$. Calculated %: N 5.58.

6. Benzyl carbethoxyleucine. To 1 g of benzylleucine in 12 ml of 1 N NaOH was added 0.55 ml of chlorocarbonic ester with cooling and stirring with a mechanical stirrer. The mixture was kept for 30 minutes with cooling and stirring. The medium was alkaline. After acidification an oil precipitated. This was removed with ether and the ether solution was dried with sodium sulfate, after which it was concentrated in a vacuum. The remaining oil did not crystallize in water, ligroin, or in organic solvents. The weight of the oil was 1.18 g (90%). On an electrochromatogram it gave a yellow spot at the point of deposition after development by benzidine.

Found %: C 65.01, 64.84; H 8.01, 8.20; N 5.13, 4.91. $C_{16}H_{23}O_4N$. Calculated %: C 65.17; H 7.91 N 4.77.

Saponification of benzyl carbethoxyleucine and isolation of benzyl carboxyleucine. To the preparation of benzyl carbethoxyleucine (0.5 g) was added 30 ml of 1 N NaOH and the mixture was heated for 17 hours on a water bath. Solution occurred. After acidification with 1 N hydrochloric acid an emulsion formed which settled out as an oil. The oil was repeatedly treated with water and dried in a vacuum desiccator over sulfuric acid. On the electrochromatogram, it gave one spot at the point of deposition after development with benzidine.

Found %: N 5.37, 5.50. $C_{14}H_{19}O_4N$. Calculated %: N 5.28.

7. Benzyl carbethoxyvalylglycylglycine ethyl ester. We dissolved 0.4 g of benzyl carbethoxyvaline in 15 ml of anhydrous chloroform in the presence of 0.20 ml of anhydrous triethylamine. To the solution, cooled with snow and salt, we added 0.14 ml of chlorocarbonic ester. The mixture was kept for 15 minutes with cooling and stirring, and the second component was then added—0.23 g of glycylglycine ethyl ester hydrochloride dissolved in anhydrous chloroform in the presence of 0.20 ml of anhydrous triethylamine. The mixture was kept in the cold for 15-20 minutes, and then overnight at room temperature. The chloroform solution was treated four times with 2 N hydrochloric acid and four times with water to a negative ninhydrin reaction. The chloroform was dried with sodium sulfate and distilled off in a vacuum. The remaining oil was dried in a vacuum desiccator over sulfuric acid. On the electrochromatogram under the conditions described above it gave a blue green spot at the point of deposition after development by benzidine and did not contain an admixture of glycylglycine ethyl ether. The biuret reaction was positive. Yield 0.47 g (80%).

Found %: N 9.68, 9.73. $C_{21}H_{31}O_6N_3$. Calculated %: N 9.98.

To confirm the structure we studied the amino acid composition by the method of paper chromatography. We carried out a 50 hour hydrolysis with 20% hydrochloric acid. On the paper chromatogram of the hydrolyzate (solvent butanol–water–acetic acid, 4 : 5 : 1), developed with ninhydrin and benzidine, we found valine and glycine.

8. Benzyl carbethoxyglycylalanylphenylalanine. a) To 0.38 g of benzyl glycylalanylphenylalanine in 20 ml of anhydrous chloroform we added 1.4 ml of anhydrous triethylamine. With cooling and stirring we added 0.09 ml of chlorocarbonic ester and allowed the mixture to stand overnight at room temperature. Then the

mixture was diluted with water and the oil which precipitated was dissolved in dilute acetic acid; the solution was allowed to stand at room temperature. After a week, the precipitated crystals were filtered off and repeatedly washed with water. The electrochromatogram in 30% CH_3COOH indicated the homogeneity of the substance. The resulting benzyl carbethoxyglycylalanylphenylalanine gave a positive biuret and a negative picric reaction, m. p. 104°. Not described in the literature.

b) One g of benzylglycylalanylphenylalanine was dissolved in 3.4 ml of 1 N NaOH and 0.25 ml of chlorocarbonic ester was added with cooling and stirring with a mechanical stirrer. The mixture stood with cooling and stirring for 30 minutes and was then acidified with hydrochloric acid and the oil which precipitated was extracted with ether. The ether solution was dried with sodium sulfate and concentrated in a vacuum to an oily residue which crystallized into a white, crystalline solid when rubbed with a rod under ligroin. M. p. 106°. Yield 0.9 g (80%). On the electrochromatogram the substance showed a yellow color and was found at the point of deposition. The resulting benzyl carbethoxyglycylalanylphenylalanine gave a positive biuret reaction and was identical in properties with the one obtained under conditions of mixed anhydrides.

Found %: C 63.53, 63.49; H 6.70, 6.78; N 8.76, 8.80. $C_{24}H_{29}O_6N_3$. Calculated %: C 63.27; H 6.42; N 9.18.

SUMMARY

1. We have synthesized the benzylaminoacids: benzylphenylalanine, -leucine, and -valine.

2. We have synthesized the undescribed benzyl carbethoxy- and benzyl carboxyamino acids: benzyl carbethoxyphenylalanine, -leucine, and -valine, benzyl carboxyleucine and -valine.

3. We have obtained the undescribed benzyltripeptide derivatives: benzyl carbethoxyglycylalanylphenylalanine and -valylglycylglycine (as esters).

4. We have shown the formation of benzyl carbethoxyamino acids in carrying out the peptide synthesis with benzylamino acids under the conditions of mixed anhydrides (with chlorocarbonic ester).

LITERATURE CITED

1. L. N. Akimova and N. I. Gavrilov, Zhur. Obshch. Khim. 27, 1299 (1957).*
2. L. N. Akimova, N. I. Gavrilov, and A. A. Akimova, Zhur. Obshch. Khim. 27, 2268 (1957).*
3. E. Fischer, Untersuchungen über Aminosäuren, Peptide und Proteine, II, 879 (1923).
4. L. Velluz, G. Amiard, and R. Heymes, Bull. Soc. Chim. 21, 1012 (1954).

* Original Russian pagination. See C. B. translation.

SOME PROPERTIES OF N-BENZYLATED PEPTIDES. IV.

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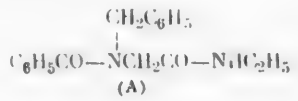
There are a number of indications in the literature of the use in peptide synthesis of a series of simultaneous protective groups, that is, as a rule, protective groups on different nitrogen atoms. Thus, in the synthesis of the peptides of gramicidin C there was simultaneous use of carbobenzoxy and tosyl, trityl and tosyl protectors [1]. As to the use of double protectors, but simultaneously on one atom of nitrogen, we have only the indication of the dibenzyl group. Compounds with two protectors have been described, such as benzoyl benzylglycylethylamide [2] (A), but they have not been used in the peptide synthesis.

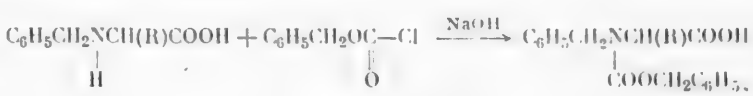


(A)

The use of two protective groups is satisfactory in the respect that in removing one of them under definite conditions the second can be retained. In a previous communication [3] we used N-benzyl-N-carboethoxy protectors for the amine group. N-Benzyl-carboethoxyamino acids obtained by us are suitable for synthesis of peptides by the method of mixed anhydrides. Thus, we have shown the possibility of using in peptide synthesis derivatives of amino acids with double protection of the amine group.

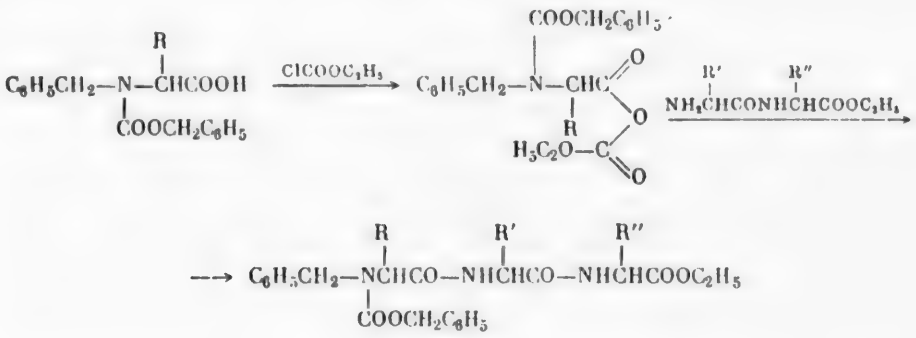
Velluz and co-workers [4] first used the method of mixed anhydrides for the synthesis with dibenzyl protectors. Peptides with monobenzyl protectors were not obtained by this method, and their synthesis was carried out by the acid chloride method. In a previous communication [3] we showed that the impossibility of the use of monobenzyl derivatives in the synthesis of peptides was connected with their easy carboethoxylation under the conditions of formation of mixed anhydrides. We tried to find conditions for getting N-benzyltetra- and pentapeptides by the method of mixed anhydrides, with preliminary protection of the hydrogen on the nitrogen in the benzyl group and thus keeping it from carboethoxylation. We followed the plan of seeking a protector which would be removed under milder conditions than for benzyl. This would make possible the retention of the benzyl group in the resulting peptide. Such a protector was the carbobenzoxy group, which is easily removed.

Thus, we first used for the synthesis of benzylpeptides a combined benzyl-carbobenzoxy protector for the amine group. For this purpose, we worked out the synthesis of N-benzyl-carbobenzoxyamino acids and peptides. It consisted in the action of carbobenzoxychloride on N-benzylamino acids or peptides in an alkaline medium. The reaction takes place according to the equation:



Carbobenzoxychloride and N-benzylamino acids were taken in equimolecular amounts. By this method, we prepared N-benzyl-carbobenzoxyphenylalanine, -leucine, and -glycylalanylphenylalanine. All the synthesized substances were obtained in yields of 80-90%. N-Benzyl-carbobenzoxyphenylalanine and -leucine were oils which

did not crystallize in water or under nonaqueous conditions. In distinction from them, N-benzyl-carbobenzoxy-glycylalanylphenylalanine was a solid substance with m. p. 94°. The preparations of N-benzyl-carbobenzoxy-amino acids were used further for the synthesis of N-benzyl-carbobenzoxytripeptides by the method of mixed anhydrides which we had already carried out on the N-benzyl-carboethoxyamino acids. The synthesis of N-benzyl-carbobenzoxytripeptides (esters) was carried out by the following scheme.



As a result we obtained the ethyl esters of N-benzyl-carbobenzoxytripeptides whose isolation and purification were carried out in a manner analogous to that of the N-benzyl-carboethoxy derivatives. Both the tripeptide esters synthesized by this method were obtained in high yield (90%) and were noncrystallizing oils, easily soluble in organic solvents and giving the biuret reaction (λ_{max} 580 mμ).

N-Benzyl-carbobenzoxyamino acids and peptides are very soluble in organic solvents, which is very important for the peptide synthesis, since it is known that the carbobenzoxy peptides (especially the higher carbobenzoxy peptides) can not be used at all in peptide synthesis by this method due to their poor solubility in organic solvents.

EXPERIMENTAL

I. Synthesis of N-Benzyl-Carbobenzoxyamino Acids and Their Derivatives

1. N-Benzyl-carbobenzoxyleucine. Two g of N-benzylleucine was dissolved in 18 ml of 1 N NaOH. With cooling and stirring an equivalent amount (1.56 g) of carbobenzoxychloride was added to the solution. After some time, precipitation occurred. The mixture was kept with cooling and stirring for 1.5 hours and remained overnight at room temperature. It was acidified with hydrochloric acid and the oil which precipitated was removed with ether. The ether solution was dried with sodium sulfate and concentrated in a vacuum. The residual oil was dried in a vacuum desiccator over sulfuric acid. On the electrochromatogram (experimental conditions: 5 hours, buffer 30% CH_3COOH, potential gradient 6.8 v/cm) after development with benzidine it gave a yellow spot at the point of deposition.

2. N-Benzyl-carbobenzoxyleucylalanylphenylalanine (ethyl ester). We dissolved 1.8 g of N-benzyl-carbobenzoxyleucine in 20 ml of anhydrous chloroform in the presence of 0.83 ml of anhydrous triethylamine. To the cooled solution we added 0.6 g of chlorocarbonic ester. The mixture was kept for 15 minutes with cooling and stirring, and the second component was then added, 1.5 g of alanylphenylalanine ethyl ester hydrochloride dissolved in anhydrous chloroform in the presence of 0.75 ml of anhydrous triethylamine. The mixture remained for 15-20 minutes in the cold, and then overnight at room temperature. The chloroform solution was treated with 2 N hydrochloric acid and then with water to a negative ninhydrin reaction in the filtrate, dried with sodium sulfate, and concentrated in a vacuum. The residual oil was dried in a vacuum desiccator over sulfuric acid. On the electrochromatogram after development with benzidine it gave a blue green spot at the point of deposition and did not contain an admixture of alanylphenylalanine ethyl ester. The biuret reaction was positive. We obtained 2.8 g (93%).

Found %: C 69.90, 69.74; H 7.03, 7.15; N 7.15, 7.03. $C_{35}H_{43}O_6N_3$. Calculated %: C 69.88; H 7.20; N 6.98.

To show the structure we carried out a study of the amino acid composition by paper chromatography. We ran a 50 hour hydrolysis of the substance with 20% hydrochloric acid. The paper chromatogram of the hydrolyzate (solvent: butanol–water–acetic acid 4 : 5 : 1), developed with ninhydrin and benzidine, showed leucine, alanine, and phenylalanine.

3. N-Benzyl-carbobenzoxyphenylalanine. One g of N-benzyl-phenylalanine was dissolved in 10 ml of 1 N NaOH. With cooling and stirring 0.85 ml of carbobenzoxychloride was added. A precipitate was formed in the alkaline medium. The mixture was kept for 40 minutes with cooling and stirring and then for one hour at room temperature. The precipitate was washed repeatedly with water, dried, and then treated with ether, upon which the N-benzyl-carbobenzoxyphenylalanine dissolved. The remaining precipitate (0.2 g) was unreacted N-benzylphenylalanine. The ether solution was concentrated in a vacuum. The residual oil was deposited on an electrochromatogram. It showed one spot at the point of deposition after benzidine development, which showed the homogeneity of the substance.

4. N-Benzyl-carbobenzoxyphenylalanylalanylphenylalanine (ethyl ester). We dissolved 1.2 g of N-benzyl-carbobenzoxyphenylalanine in 18 ml of anhydrous chloroform in the presence of 0.41 ml of anhydrous triethylamine. To the cooled solution, we added 0.35 g of chlorocarbonic ester. The mixture was kept for 15 minutes with cooling and stirring, after which the second component was added –0.95 g of alanylphenylalanine ethyl ester hydrochloride dissolved in anhydrous chloroform in the presence of 0.45 ml of anhydrous triethylamine. Isolation was carried out as described above. On the electrochromatogram the substance gave a blue-green spot at the point of deposition after development with benzidine, and contained no admixture of alanylphenylalanine ethyl ester. The resulting ethyl ester of N-benzylcarbobenzoxyphenylalanylalanylphenylalanine gave a positive biuret reaction. Yield 1.73 g (91%).

Found %: C 71.60, 71.45; H 6.43, 6.49; N 5.90, 6.07. $C_{38}H_{41}O_6N_3$. Calculated %: C 71.81; H 6.45; N 6.59.

For confirmation of the structure we studied the amino acid composition by the method of paper chromatography. We ran a 48-hour hydrolysis of the substance with 20% hydrochloric acid. On the paper chromatogram of the hydrolyzate (solvent: butanol – water–acetic acid 4 : 5 : 1) developed with ninhydrin and benzidine we observed phenylalanine and alanine.

II. Synthesis of N-Benzyl-Carbobenzoxytripeptides

1. N-Benzyl-carbobenzoxyglycylalanylphenylalanine. To 1 g of N-benzyl-glycylalanylphenylalanine dissolved in 3.4 ml of 1 N NaOH was added with cooling and stirring 0.45 ml of carbobenzoxychloride. After 40 minutes the solution was acidified with hydrochloric acid and the oil which precipitated was extracted with ether. The ether solution was dried with sodium sulfate and the ether was distilled off. The remaining oil crystallized under ligroin. The resulting precipitate was filtered and dried in a vacuum desiccator over sulfuric acid. M. p. 94°. Not described in the literature. Yield 1.1 g (84%). Biuret reaction positive. On the electrochromatogram it showed a yellow spot at the point of deposition.

Found %: C 66.89, 66.90; H 6.14, 6.21; N 7.79, 7.70. $C_{29}H_{31}O_6N_3$. Calculated %: C 67.28; H 6.04; N 8.13.

For confirmation of the amino acid composition we ran a 50-hour hydrolysis of the substance. On the paper chromatogram of the hydrolyzate with ninhydrin development we observed glycine, alanine, and phenylalanine.

2. N-Benzyl-carbobenzoxyleucylalanylphenylalanine. To a cooled solution of 1 g of N-benzyl-leucylalanylphenylalanine in 7.5 ml of 1 N NaOH we added with stirring 0.73 ml of carbobenzoxychloride. After 30 minutes the alkaline solution was acidified with hydrochloric acid and the oil which formed was extracted with ether. After drying over sodium sulfate, the ether was distilled off and the remaining oil was repeatedly treated with ligroin until the odor of carbobenzoxychloride disappeared (decantation). The residual oil in a vacuum desiccator over P_2O_5 crystallized. M. p. 69-70°. Not described in the literature. Yield 0.9 g (70%). Easily soluble in alcohol, ether, chloroform, and other organic solvents. Hygroscopic. Biuret reaction positive.

Found %: C 69.05, 68.97; H 7.30, 7.27; N 7.12, 7.19. $C_{33}H_{39}O_6N_3$. Calculated %: C 69.08; H 6.85; N 7.32.

To test the homogeneity of the substance it was placed on an electrochromatogram in 30% CH_3COOH at a potential gradient of 6 v/cm for 6 hours. After development with benzidine it showed one spot at the point of deposition. On a descending chromatogram (solvent, aqueous butanol) we observed one spot with $R_f = 0.90$ (developer, benzidine).

3. N-Benzyl-carbobenzoxyleucylglycylglycine. To a solution of 1 g of N-benzyl-leucylglycylglycine in 9 ml of 1 N NaOH we added with cooling and stirring 0.96 ml of carbobenzoxychloride. The treatment was analogous to that for N-benzyl-carbobenzoxyleucylalanylphenylalanine. The oil could not be crystallized. Yield 0.65 g (92%). Not described in the literature. Easily soluble in organic solvents, hygroscopic. Biuret reaction positive. Homogeneity confirmed by electrophoresis. One spot shown by benzidine development. On a descending chromatogram (solvent, aqueous butanol) with benzidine development it showed one spot with $R_f = 0.92$.

4. N-Benzyl-carbobenzoxyvalylglycylglycine. To a solution of 0.5 g of N-benzyl-valylglycylglycine in 4.5 ml of 1 N NaOH we added with stirring and cooling 0.5 ml of carbobenzoxychloride. The reaction was complete after five hours at room temperature. Treatment was analogous to that described above. The oil was repeatedly treated with ligroin. Yield 0.4 g (56%). The substance was easily soluble in alcohol, ether, and chloroform. Biuret reaction positive. For a test of homogeneity, the substance was placed on an electrochromatogram in 30% CH_3COOH for 6 hours. After benzidine development it showed one spot at the place of deposition. On a descending chromatogram (solvent, aqueous butanol) it showed one spot with $R_f = 0.90$.

III. Use of N-Benzyl-Carbobenzoxytripeptides in the Synthesis of Peptides

The combination of N-benzyl-carbobenzoxytripeptides with esters of amino acids and dipeptides was carried out analogously with the synthesis of peptides by the method of mixed anhydrides.

Ethyl ester of a tetrapeptide (N-benzyl-carbobenzoxyleucylalanylphenylalanylglycine). We dissolved 0.56 g of N-benzyl-carbobenzoxyleucyalanylphenylalanine in anhydrous chloroform and added 0.2 ml of triethylamine. To the solution, cooled to 0°, we added 0.13 ml of chlorocarbonic ester. After 10 minutes we added in portions with stirring 0.13 g of glycine ethyl ester hydrochloride in anhydrous chloroform and 0.2 ml of triethylamine. The mixture was kept cold for one hour and stood overnight at room temperature. The chloroform solution was treated successively with 1 N hydrochloric acid, water, 3% sodium bicarbonate solution, and again with water to negative ninhydrin reaction in the wash solution, dried over ignited sodium sulfate, and concentrated in a vacuum. The resulting oil could not be crystallized. Yield 0.54 g (85%). Soluble in alcohol, chloroform, and gives a positive biuret reaction.

Found %: N 8.25, 8.34. $C_{37}H_{46}O_7N_4$. Calculated %: N 8.50.

SUMMARY

1. We have synthesized the following N-benzyl-carbobenzoxytripeptides: N-benzyl-carbobenzoxy-glycylalanylphenylalanine, -leucylalanylphenylalanine, -leucylglycylglycine, and -valylglycylglycine.

2. We have shown the possibility of using N-benzyl-carbobenzoxytripeptides in peptide synthesis by the method of mixed anhydrides in the example of the ethyl ester of a tetrapeptide.

LITERATURE CITED

1. R. Schwyzer and P. Suber, Angew. Chem. 68, 518 (1956).
2. C. Granacher, G. Wolf, and A. Weidinger, Helv. Chim. Acta 11, 1228 (1928).
3. L. N. Akimova, Zhur. Obshch. Khim. 30, 1143 (1960).*
4. L. Velluz, I. Anatol, and G. Amiard, Bull. Soc. Chim. 23, 201 (1956).

* Original Russian pagination. See C. B. translation.

HEXAMETHYLENEIMINE DERIVATIVES

V. ESTERS OF β-N-HEXAMETHYLENE AMINOETHYL ALCOHOL

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In previous communications of this series we have shown that hexamethyleneimine is a very reactive substance, entering into reactions with various halogen compounds with formation of tertiary amines [1], amides [2], and esters of N-hexamethylene amino acids [3]. Using the ability of hexamethyleneimine to react easily with halogen compounds, we have tried to obtain esters of β-N-hexamethylene aminoethyl alcohol by reaction of the esters of β-chloroethyl alcohol with hexamethyleneimine.

$$RCOOCH_2CH_2Cl + 2(CH_2)_6NH \rightarrow RCOOCH_2CH_2N(CH_2)_6 + (CH_2)_6NH \cdot HCl.$$

The synthesis of esters of β-N-hexamethylene aminoethyl alcohol is also of interest because among these compounds there could be substances with anesthetizing action like other compounds of the general formula $RCOOCH_2CH_2NR'_2$. The constants of the esters of β-N-hexamethylene aminoethyl alcohol which we have obtained are given in the table.

Acid group in ester of β-N-hexamethylene aminoethyl alcohol	Temperature (pressure in mm)	n_D^{20}	d_4^{20}
Formic	120—122° (6)	1.4217	1.0320
Acetic	164—166 (6)	1.4812	1.0102
n-Butyric	143—144 (8)	1.4432	1.0072
Methacrylic	99—101 (7)	1.3949	0.9843
Phenylacetic	240—242 (3)	1.6451	1.1456
Benzoic	210—211 (6)	1.4641	1.0014
Salicylic	184—186 (2)	1.5271	1.0251
4-Methoxybenzoic	143—144 (7)	1.3940	1.0710
2,4-Dichlorobenzoic	173—174 (4)	1.4932	1.1401

EXPERIMENTAL

Method of performing the experiments. A solution of hexamethylene imine in benzene or toluene was placed in a three-necked flask fitted with a stirrer, reflux condenser, and dropping funnel, and to it was gradually added with stirring the β-chloroethyl ester of the corresponding acid. The reaction mixture was heated on a boiling water bath for two to three hours and allowed to stand overnight. The crystals of hexamethyleneimine hydrochloride were filtered off, the solvent was distilled from the solution, and the residue was distilled in a vacuum. The separated esters of β-N-hexamethylene aminoethyl alcohol were repeatedly distilled in a vacuum.

β-N-hexamethylene aminoethyl formate was obtained from 165 g of hexamethyleneimine in 250 ml of toluene and 80 g of β-chloroethyl formate (b. p. 127-128°, $n^{20}D$ 1.2740, d^{20}_{20} 1.016); yield 45 g (35%).

Found %: N 8.36, 8.29. $C_9H_{17}O_2N$. Calculated %: N 8.18.

Picrate, m. p. 123-124° (from alcohol).

Found %: N 13.94, 13.87. $C_{15}H_{20}O_9N_4$. Calculated %: N 14.00.

β-N-hexamethylene aminoethyl acetate was obtained from 140 g of hexamethyleneimine in 250 ml of toluene and 80 g of β-chloroethyl acetate (b. p. 145°, $n^{20}D$ 1.4810, d^{20}_{20} 1.1742); yield 54 g (44%).

Picrate, m. p. 163-164° (from alcohol).

Found %: N 13.54, 13.39. $C_{16}H_{22}O_9N_4$. Calculated %: N 13.52.

β-N-hexamethylene aminoethyl n-butyrate was obtained from 56 g of hexamethyleneimine in 100 ml of toluene and 36 g of β-chloroethyl n-butyrate (b. p. 82-84° at 4 mm, $n^{20}D$ 1.4250, d^{20}_{20} 1.0691); yield 34 g (67%).

Picrate, m. p. 156-157° (from alcohol).

Found %: N 12.83, 12.58. $C_{18}H_{26}O_9N_4$. Calculated %: N 12.67.

β-N-hexamethyleneaminoethyl methacrylate was obtained from 230 g of hexamethyleneimine in 250 ml of benzene and 175 g of β-chloroethyl methacrylate ($n^{20}D$ 1.2353, d^{20}_{20} 1.0430); yield 117 g (45 %).

β-N-hexamethylene aminoethyl phenylacetate was obtained from 56 g of hexamethyleneimine in 100 ml of toluene and 53 g of β-chloroethyl phenylacetate (b. p. 137-139° at 7 mm, $n^{20}D$ 1.5460, d^{20}_{20} 1.1580); yield 35 g (45%).

Picrate, m. p. 172° (from alcohol).

Found %: N 11.22, 11.31. $C_{22}H_{26}O_9N_4$. Calculated %: N 11.43.

β-N-hexamethylene aminoethyl benzoate was obtained from 112 g of hexamethyleneimine in 250 ml of toluene and 65 g of β-chloroethyl benzoate (b. p. 259-260°, $n^{20}D$ 1.3782, d^{20}_{20} 1.0741); yield 42.5 g (49%).

Picrate, m. p. 139° (from alcohol).

Found %: N 12.08, 11.84. $C_{21}H_{24}O_9N_4$. Calculated %: N 11.76.

β-N-hexamethylene aminoethyl salicylate was obtained from 65 g of hexamethyleneimine in 100 ml of benzene and 64 g of β-chloroethyl salicylate (b. p. 137-139° at 7 mm, $n^{20}D$ 1.3990, d^{20}_{20} 1.0171); yield 14 g (16.7%).

Picrate, m. p. 176° (from alcohol).

Found %: N 11.24, 11.29. $C_{21}H_{24}O_{10}N_4$. Calculated %: N 11.38.

β-N-hexamethylene aminoethyl 4-methoxybenzoate was obtained from 20 g of hexamethyleneimine in 50 ml of toluene and 22 g of β-chloroethyl 4-methoxybenzoate (b. p. 194-196° at 7 mm, $n^{20}D$ 1.3372, d^{20}_{20} 1.1041); yield 13.7 g (48%).

Picrate, m. p. 123-124° (from alcohol).

Found %: N 11.32, 11.24. $C_{22}H_{26}O_{10}N_4$. Calculated %: N 11.06.

β-N-hexamethylene aminoethyl 2,4-dichlorobenzoate was obtained from 54 g of hexamethyleneimine in 100 ml of toluene and 45 g of β-chloroethyl 2,4-dichloroethylbenzoate (b. p. 142-144° at 4 mm, $n^{20}D$ 1.3911, d^{20}_{20} 1.1049); yield 24 g (43%).

Picrate, m. p. 154° (from alcohol).

Found %: N 10.49, 10.53. $C_{21}H_{22}O_9N_4Cl_2$. Calculated %: N 10.28.

SUMMARY

We have synthesized and characterized nine esters of β-N-hexamethylene aminoethyl alcohol which have not been described in the literature.

LITERATURE CITED

1. G. S. Kolesnikov and N. N. Mikhailovskaya, Zhur. Obshch. Khim. 27, 458 (1957);* G. S. Kolesnikov and L. I. Shcherbo, Zhur. Obshch. Khim. 28, 519 (1958).*
2. G. S. Kolesnikov, T. V. Smirnova, L. I. Mizrakh, N. N. Mikhailovskaya, and L. I. Shcherbo, Zhur. Obshch. Khim. 27, 3005 (1957).*
3. G. S. Kolesnikov and T. A. Kabanova, Khimiya i Khim. Tekhnol. NIVSh (1958), p. 66.

* Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF XYLOCAINE

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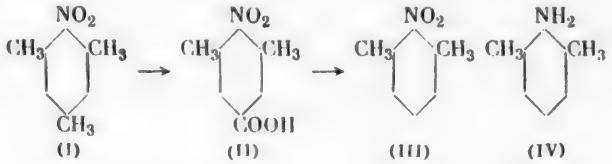
The local anesthetic xylocaine, introduced into medical practice abroad, is α-diethylaminoacetyl-2,6-dimethylaniline hydrochloride. Xylocaine has all the aspects of a local anesthetic, long action, and slight toxicity, which actually distinguished it from other local anesthetics [1]. The synthesis of xylocaine and its analogs has been the subject of a number of studies of which we cite two reviews in the bibliography [2, 3]. The preparation of xylocaine involves the use of the difficultly obtained vicinal m-xylidine (2,6-dimethylaniline) since the introduction of the amino group between the two methyl groups of m-xylene results in small yields of vicinal m-xylidine because of spacial difficulties [4, 5]. The latter can be isolated from a technical mixture of xylidines (its content in this mixture, according to [4], is 2-3%). A method has been described for nitration of m-xylene under conditions which permit getting a higher yield of 2,6-dimethylnitrobenzene [6], the intermediate product for getting vicinal m-xylidine. Patents have been granted on processes for isolation of this substance from mixtures of xylidines [7, 8].

We have tried to obtain vicinal m-xylidine by the method described in [9]. However, because of the absence of experimental data in the report, we have not been able to repeat the synthesis. Moreover, this method involves the use of hydrogen sulfide. In seeking a suitable path for synthesis of vicinal m-xylidine, we felt it expedient to try to obtain it by removal of a methyl group in nitromesitylene, which is a commercial product of the domestic chemical industry. Nitromesitylene has been oxidized into 3,5-dimethyl-4-nitrobenzoic acid [10, 11] which then in the presence of a catalyst undergoes decarboxylation.



We obtained the best results by carrying out the decarboxylation reaction in a medium of quinoline at its boiling point and in the presence of a mixture of copper powder and copper-chromium catalyst. By the reduction of the resulting 2,6-dimethylnitrobenzene by iron filings in dilute acetic acid we obtained vicinal m-xylidine which was characterized by its acetyl, formyl, and chloroacetyl derivatives. From the latter compound by the usual method described in the literature (replacing the chlorine of the chloroacetamide group by the diethylamino group) we obtained α-diethylaminoacetyl-2,6-dimethylaniline. When hydrogen chloride acted on it, it gave the corresponding hydrochloride. The xylocaine obtained in this way was identical in its physicochemical and pharmacological properties with xylocaine described in [1].

In the production of nitromesitylene by nitration of mesitylene with nitric acid we can expect formation of nitromesitylenic acid as a by-product, as a result of the oxidizing action of nitric acid. From this by-product of the reaction we can obviously isolate 3,5-dimethyl-4-nitrobenzoic acid needed for the synthesis of vicinal m-xylidine.

EXPERIMENTAL

3,5-Dimethylnitrobenzoic acid (II) was obtained by oxidizing 40 g of nitromesitylene (I) with 28 g of chromic anhydride in acetic acid [10]. Yield 6.2 g (43.5%), m. p. 215° (from absolute alcohol). We recovered 28 g of nitromesitylene.

2,6-Dimethylnitrobenzene (III). We heated 11.8 g of (II), 0.5 g of copper-chromium catalyst, and 0.15 g of copper powder in 30 ml of dry redistilled quinoline in a flask fitted with a reflux air condenser. At about 210° evolution of bubbles of carbon dioxide gas began. The temperature was increased to the boiling point of quinoline and the mixture was boiled for four hours. After cooling, the reaction mass was acidified to an acid reaction to Congo with dilute (1:1) hydrochloric acid, and 2,6-dimethylnitrobenzene was distilled with steam. The distillate was extracted several times with ether, the ether extract was dried with calcium chloride and the ether was distilled off. The residue was distilled at ordinary pressure. We obtained 5.05 g (54.5%) of a light yellow oil, b. p. 223° at 754 mm; according to the data of [12], b. p. 225° at 744 mm.

2,6-Dimethylaniline (vicinal m-xylidine) (IV). We placed 5.0 g of (III), 20 ml of acetic acid, and 10 ml of water in a three-necked flask fitted with a stirrer and reflux condenser. The mixture was heated on a boiling water bath and over 8 hours with good stirring we added 5 g of iron filings in small portions. After addition of the filings, the water in the bath was saturated with salt, and the reaction mass was heated for two hours more without stopping the stirring. The cooled mixture was made alkaline with calcined soda and distilled with steam. The distillate was saturated with sodium chloride and extracted with ether. The ether extract was dried with ignited potash and after distillation of the ether the residue was distilled at ordinary pressure. We obtained 3.52 g (88%) of light yellow oil, b. p. 212-213° at 737 mm, $n^{20}D$ 1.561 (literature data: $n^{20}D$ 1.558 [9], b. p. 214° at 739 mm [12]).

Acetyl derivative, m. p. 176.5°.

Found %: C 73.73, 73.79; H 8.12, 8.08. $C_{10}H_{13}ON$. Calculated %: C 73.53; H 8.03.

Formyl derivative, m. p. 163° (slow melting). According to the literature data: m. p. 164-165° (slow melting), m. p. 176-177° (rapid melting) [13]. Marcus et al. give m. p. 164-165° [9].

α-Chloroacetyl-2,6-dimethylaniline, m. p. 144.5-146°; according to [1], m. p. 146°.

α-Diethylaminoacetyl-2,6-dimethylaniline (xylocaine). A solution of 1.4 g of chloroacetyl-2,6-dimethylaniline and 1.7 g of diethylamine in 15 ml of anhydrous toluene was heated for three hours in a flask with a reflux condenser. After cooling, the solution was filtered from diethylamine hydrochloride, toluene and excess diethylamine were distilled off in the vacuum of the water pump, and the residue was dissolved in 10% hydrochloric acid. The hydrochloric acid solution was treated with activated charcoal, filtered, and the filtrate was made alkaline. The oil which separated was extracted with ether. The ether extract was dried with ignited potash and the ether was distilled off. The residue quickly crystallized. We obtained 1.4 g (85%) of an almost colorless substance with m. p. 62-63°; after recrystallizing from aqueous alcohol and drying over phosphoric anhydride in a vacuum it melted at 67-69° (according to [1]: m. p. 68-69°). The hydrochloride was obtained by addition of an ether solution of hydrogen chloride to the ether solution of α-diethylaminoacetyl-2,6-dimethylaniline. It was twice recrystallized from a mixture of ethyl acetate and alcohol and dried in a vacuum at 100° over phosphoric anhydride and melted at 127-128° (according to [1]: m. p. 128-129°). It is interesting that after careful drying under these conditions, xylocaine loses its hygroscopicity.

Found %: C 62.05, 62.08; H 8.76, 8.62; N 10.65, 10.53. $C_{14}H_{23}ON_2Cl$. Calculated %: C 62.09; H 8.56; N 10.35.

SUMMARY

We have found a new path for the synthesis of xylocaine, starting from 3,5-dimethyl-4-nitrobenzoic acid.

LITERATURE CITED

1. N. Löfgren, Arkiv. Kemi Mineral. Geol. A 22, 30 (1946); Chem. Abs. 43, 1021 (1949).

2. A. Calicetl, Corriere farmac. 12, 86 (1957).
3. T. P. Carney, Rec. Chem. Progr. 15, 143 (1954).
4. A. Fedorov and A. Spryskov, Prom. Org. Khim. 3, 396 (1937).
5. E. Nolting and S. Forel, Ber. 18, 2675 (1885).
6. A. K. Kenneth and H. M. Brennecke, Ind. Eng. Chem. 46, 728 (1954).
7. British Patent 327,830 (1930); Zbl. (1930), II, 800.
8. British Patent 382,418 (1930); Zbl. (1930), II, 982.
9. J. Marcus, A. Bardeanu, and Z. Teodoresku, Rev. Chim. 7, 109 (1956).
10. B. C. Sanders and G. H. R. Watson, Biochem. J. 46, 629 (1950).
11. Peter. P. T. Sach and Pu Lin, J. Chinese Chem. Soc. 14, 94 (1946).
12. Dictionary of Organic Compounds (1949), Vol. 3.
13. Beilst. 12, 1109 (1929).

2-(o-HYDROXYPHENYL)-BENZIMIDAZOLE

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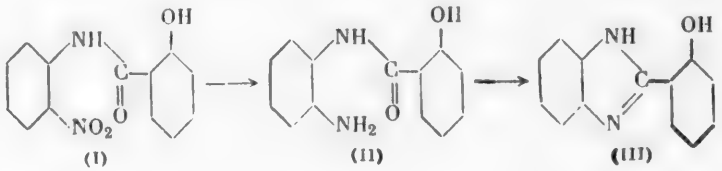
In the reduction of the o-nitroanilide of salicylic acid (I) by tin in the presence of hydrochloric acid, Hübner [1] obtained as the final reaction product 2-(o-hydroxyphenyl)-benzimidazole (III). The yield of product was not given, only the melting point of 222.5°. We can assume that the reaction takes place through an intermediate stage of formation of the o-aminoanilide of salicylic acid (II).



(I) (II) (III)

However, compound (II) has not been isolated until now. Probably under the conditions of running the reaction the o-aminoanilide of salicylic acid (II) formed in the reduction under the influence of hydrochloric acid undergoes the reaction usual for such compounds leading to intramolecular condensation with closure of the imidazole ring and formation of 2-(o-hydroxyphenyl)-benzimidazole.

In the reduction of the o-nitroanilide of salicylic acid by sodium hydrosulfite in an alkaline medium we succeeded in stopping the reduction reaction; we thus obtained a 30% yield of the o-amino anilide (II) in the form of white crystals which melted at 156°. When boiled with hydrochloric acid this amino compound was quantitatively converted into 2-(o-hydroxyphenyl)-benzimidazole which melted at 239°.

We repeated the reduction of the o-nitroanilide by tin according to Hübner and thus obtained a product with a lower melting point which slowly rose after repeated recrystallizations from alcohol. After a supplementary purification of the product by solution in alkali and precipitation from solution by acetic acid with later recrystallization from alcohol we obtained 2-(o-hydroxyphenyl)-benzimidazole with m. p. 239-240°. 2-(o-Hydroxyphenyl)-benzimidazole was also obtained by condensation of salicylamide with o-phenylenediamine; the yield on this reached 30%; the melting point was 242° [2].

We studied the possibility of using other salicylic acid derivatives for the synthesis of 2-(o-hydroxyphenyl)-benzimidazole. A very good result was obtained in the reaction of o-phenylenediamine with the phenyl ester of salicylic acid (salol) by the method which we used for obtaining various arylides of salicylic acid [3]. When we fused a mixture of equimolecular amounts of salol and o-phenylenediamine for 5-6 hours at 180°, we obtained 2-(o-hydroxyphenyl)-benzimidazole of high purity in a yield of 90%. It is worthy of attention that the reaction of o-phenylenediamine with methyl salicylate occurs with strong tarring and the yield of the final product does not surpass 15%. Assuming that a high yield of product using salol is favored by the phenol formed in the reaction, we carried out the condensation of o-phenylenediamine with salicylic acid itself in boiling phenol; however, in this case the yield of 2-(hydroxyphenyl)-benzimidazole did not reach 5%. An analogous result was obtained in the use of other high boiling solvents (isoamyl alcohol, naphthalene).

A considerably better effect was obtained in the reaction of o-phenylenediamine with salicylic acid in the presence of some dehydrating media. In the use of phosphorus pentachloride the yield of 2-(o-hydroxyphenyl)-benzimidazole reached 30%, with phosphorus trichloride, 70%, and with phosphorus pentoxide, over 90%. In the last case, the reaction was carried out in the absence of a solvent and was completed in 10-15 minutes. Such a process, equal to that with salol, can be recommended for preparative securing of 2-arylbenzimidazoles.

2-(o-Hydroxyphenyl)-benzimidazole is obtained after recrystallization from benzene in the form of colorless, well formed plates, from alcohol in the form of white needles which melt sharply at 239-240°. The blue-violet fluorescence of the alkaline solution of this compound is noteworthy, while the acid solution does not fluoresce. This permits us to use 2-(o-hydroxyphenyl)-benzimidazole as a fluorescent indicator in the titration of colored or opaque solutions with illumination by ultraviolet light [4].

2-(o-Hydroxyphenyl)-benzimidazole gives salts with both acids and bases. The alkali salts of the compound are easily soluble in water while solution of the hydrochloride in water produces hydrolysis and precipitation of the hydroxyphenylbenzimidazole base.

The spacial nearness in 2-(o-hydroxyphenyl)-benzimidazole of the hydroxyl group and the nitrogen atom of the heterocyclic nucleus make possible reaction with ions of heavy metals with the formation of intramolecular complexes. According to the literature [4], 2-(o-hydroxyphenyl)-benzimidazole is used for the isolation of mercury from solutions of its salts.

EXPERIMENTAL

Salicylic acid o-nitroanilide. Equimolecular amounts of o-nitroaniline and salol were fused at 180° for 8 hours. When the melt had cooled, it was dissolved in alkali. The product was precipitated from solution by acetic acid, filtered, washed with hot water, and recrystallized from alcohol. Yield 60%, m. p. 156°.

Salicylic acid o-aminoanilide. Twenty g of salicylic acid o-nitroanilide was dissolved in 250 ml of 10% sodium hydroxide, 500 ml of water was added, and the solution was heated to 80°. To the hot orange solution was added in portions 22 g of sodium hydrosulfite, and the solution became decolored. It was filtered and acetic acid was added to precipitate salicylic acid o-aminoanilide. After recrystallization from alcohol the o-aminoanilide was obtained in the form of colorless needles with m. p. 156-157°.

Found %: N 12.34, 12.46. $C_{13}H_{12}O_2N_2$. Calculated %: N 12.29.

2-(o-Hydroxyphenyl)-benzimidazole. a) Salicylic acid o-aminoanilide was boiled in hydrochloric acid solution for two hours. Then the excess acid was neutralized with alkali. The precipitated product after recrystallization from alcohol melted at 238-239°. Yield quantitative.

b) Equimolecular amounts of o-phenylenediamine and salol were fused for five hours at 180°. The phenol which separated in the reaction was distilled off and the melt was dissolved in 10% alkali. From the alkaline solution by addition of acetic acid we separated 2-(o-hydroxyphenyl)-benzimidazole. Yield 90%. After recrystallization from alcohol the product melted at 238-239°.

Found %: N 13.19, 13.32. $C_{13}H_{10}ON_2$. Calculated %: N 13.33.

c) Equimolecular amounts of salicylic acid, o-phenylenediamine, and phosphoric anhydride were carefully mixed in a round-bottomed flask and the mixture was heated until reaction began. Further heating was not used, since the condensation reaction proceeded with evolution of a large amount of heat. The resulting melt was dissolved in sodium hydroxide, and from the solution 2-(o-hydroxyphenyl)-benzimidazole was precipitated with acetic acid. Yield about 90%; after recrystallization from alcohol, m. p. 238-239°.

SUMMARY

1. By reduction of salicylic acid o-nitroanilide with sodium hydrosulfite in an alkaline solution we have obtained salicylic acid o-aminoanilide, which by heating with hydrochloric acid is cyclized to the imidazole ring with formation of 2-(o-hydroxyphenyl)-benzimidazole.

2. To obtain 2-(o-hydroxyphenyl)-benzimidazole preparatively it is more satisfactory to fuse o-phenylenediamine with salol or with salicylic acid in the presence of phosphorus pentoxide.

LITERATURE CITED

1. H. Hübner, Lieb. Ann. 210, 328 (1881).
2. J. L. Walter and H. Freiser, Anal. Chem. 25, 127 (1953).
3. I. S. Ioffe and M. Z. Zal'manovich, Zhur. Obshch. Khim. 29, 2682 (1959).*
4. Zavis Holzbecher, Chem. Listy 55, 425 (1958).

*Original Russian pagination. See C. B. translation.

EXCHANGE REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENE HYDROCARBONS

I. REACTIONS BETWEEN SOME LOWER TELOMERS OF DIENE HYDROCARBONS AND AMINES

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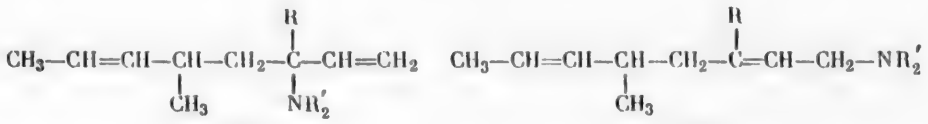
In a number of communications from our laboratory we have described reactions of telomers of divinyl, isoprene, piperylene, and chloroprene with piperylene hydrochloride (2-chloro-3-pentene), the characteristic of which is the formation of considerable amounts of lower telomers, that is, simple adducts of 2-chloro-3-pentene to dienes. In their structures they are isomers, homologs, or analogs of geranyl chloride [1].

In the literature in recent years much attention has been devoted to the behavior of allyl halogen derivatives in various reactions of nucleophilic substitution [2]. The adducts of 2-chloro-3-pentene to dienes are also, in their structures, allyl halogen derivatives. Therefore, it was interesting to study their relation to nucleophilic reagents, especially to primary and secondary amines. As a result of these reactions, here we can expect formation of two types of compounds with different arrangements of the double bonds (A and B).



(A) (B)

It was previously shown that for estimation of the nature of the multiple bonds in the telomer molecule we could successfully use the infrared spectra. We also used this method in the present work. The conclusions on the structure of the products of exchange reactions between telomers and primary and secondary amines were made on the basis of analysis of infrared spectra in the regions 1650-1670, 900-1000, and about 6100 cm^{-1}. As is known, the vinyl group (isomer A) has a frequency of valence oscillation for the double bond of about 1640 cm^{-1} and two frequencies of deformation CH- oscillation in the region 900-1000 cm^{-1}. Also very characteristic for these groups is a harmonic at about 6100 cm^{-1}. The double bond in compounds of the second type $-CH=CH-$ (isomer B) has corresponding frequencies 1660 and 960-970 cm^{-1}. The harmonic in this compound for the region 6100 cm^{-1} is absent.

The work was carried out with three amines–diethylamine, dibutylamine, and butylamine–and four telomers of 2-chloro-3-pentene with divinyl, isoprene, piperylene, and chloroprene.

In the telomerization of 2-chloro-3-pentene with divinyl we obtained in very similar amounts both possible allyl isomers (I and II).

$CH_3-CH=CH-\underset{\underset{CH_3}{|}}{CH}-CH_2-CHCl-CH=CH_2$ (I)

$CH_3-CH=CH-\underset{\underset{CH_3}{|}}{CH}-CH_2-CH=CH-CH_2Cl$ (II)

Hence, in this case we can study the exchange reaction with each telomer separately.

The experiments showed that the allyl isomers (I) and (II) with secondary amines form the same reaction product of type B. The double bond in the infrared spectrum of the reaction product has only one very weak frequency of 1662 cm^{-1} and one intense deformation frequency at 973 cm^{-1}. The harmonic at 6100 cm^{-1} was not found.

Hence, reaction with isomer (I) goes according to type $S_N'2$, that is, is accompanied by a rearrangement, and with isomer (II) according to type S_N2 (without rearrangement).

The addition of 2-chloro-3-pentene to isoprene, piperylene, and chloroprene occurs chiefly in the 1,4-position with formation of an analog of geranyl chloride.

$CH_3-CH=CH-\underset{\underset{CH_3}{|}}{CH}-CH_2-\underset{\underset{R'}{|}}{C}=CH-\underset{\underset{R''}{|}}{CHCl}$ (III)

$R' = H$, CH_3 or Cl;
$R'' = H$ or CH_3.

All these telomers with secondary amines give only products of type B with formulas and constants given in the table.

In the infrared spectra of these amines the valence oscillation of the double bond corresponds to a frequency of 1655-1665 cm^{-1} and the deformation oscillation shows an intense band at 960-965 cm^{-1} (two $-CH=CH-$ bonds).

Amines obtained with chloroprene telomers have one frequency at 1650 cm^{-1}. The valence oscillations of two different multiple bonds ($-CH=CH-$ and $-CH=CCl-$) are not differentiated. The band at 965 cm^{-1} (one bond $-CH=CH-$) has less intensity than in the other cases.

At 6100 cm^{-1} in all the compounds no absorption was found. The oscillation of $C-N$ in all cases corresponds to a band in the region 1060-1100 cm^{-1}.

The structure of the amines (X - XII) (table) obtained from telomers of 2-chloro-3-pentene with piperylene cannot be shown by infrared spectra, since both allyl isomers here have two repeated double bonds. The conclusion as to the structure of these substances was made by analogy.

Thus, as the result of this study, it was established that the adducts of 2-chloro-3-pentene with diene hydrocarbons in the exchange reaction with secondary amines form the crotyl type B independent of the structure of the amine.

In the reaction of allyl chlorides (I) and (II) with butylamine we obtained different substances. Isomer (II) gave a substance with a narrow boiling range (2°) whose spectrum contained intense bands of an amine with structure of type B (967 and 1668 cm^{-1}). Isomer (I) gave a substance with a wide boiling range in whose spectrum, besides the frequencies of an amine of type B (1668 and 967 cm^{-1}), also showed frequencies of the vinyl group (1640, 930, and 998 cm^{-1}). In the region of 6100 cm^{-1} in both cases there was a harmonic (more intense in the second case).

In an analogous way in the spectrum of the reaction product of the telomer of 2-chloro-3-pentene with butylamine, along with bands of the group $-CH=CH-$, we also found bands of the divinyl group (998 and 6100 cm^{-1}).

The telomer of chloroprene with butylamine gave only a product of type B. Frequencies of the vinyl group were absent from the spectrum.

Constants and Analyses of the Prepared Amines

Substance No.	Substance	B.p. (pressure 10 mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Found, % C	Found, % H	Found, % N	Found, % Cl	Calculated, % C	Calculated, % H	Calculated, % N	Calculated, % Cl
I	$CH_3CH{=}CHCH(CH_3)CH{=}CHCH_2N(C_2H_5)_2$	102—103°	0.8063	1.4560	65.86	65.24	79.90, 80.00	12.89, 12.98	7.18, 7.37	— —	79.93	12.90	7.17	—
II	$CH_3CH{=}CHCH(CH_3)CH{=}CHCH_2N(C_4H_9)_2$	146—147	0.8132	1.4578	84.34	83.71	81.40, 81.41	13.32, 13.42	5.89 6.25	— —	81.20	13.23	5.57	—
III	$CH_3CH{=}CHCH(CH_3)CH{=}CHCH_2NHC_4H_9$	120—121	0.8172	1.4590	65.61	64.90	79.57, 79.89	12.75, 12.91	7.82 8.00	— —	79.93	12.90	7.17	—
IV	$CH_3CH{=}CHCH(CH_3)C(CH_3){=}CHCH_2N(C_2H_5)_2$	109.5—110.5	0.8143	1.4602	70.45	69.86	80.16, 80.61	12.83, 13.01	7.07 7.11	— —	80.31	13.00	6.69	—
V	$CH_3CH{=}CHCH(CH_3)C(CH_3){=}CHCH_2N(C_4H_9)_2$	152—153	0.8191	1.4610	88.93	88.33	81.40, 81.54	13.33, 13.40	5.37 5.38	— —	81.43	13.29	5.28	—
VI	$CH_3CH{=}CHCH(CH_3)C(CH_3){=}CHCH_2NHC_4H_9$	124—125	0.8193	1.4620	70.25	69.52	79.59, 80.05	13.00, 13.05	6.63 7.18	— —	80.31	13.00	6.69	—
VII	$CH_3CH{=}CHCH(CH_3)C(Cl){=}CHCH_2N(C_2H_5)_2$	120—121	0.9101	1.4710	70.57	70.11	67.09, 67.29	10.42, 10.48	6.69 6.94	15.32 15.85	67.94	10.53	6.10	15.43
VIII	$CH_3CH{=}CHCH(CH_3)C(Cl){=}CHCH_2N(C_4H_9)_2$	161—162	0.8936	1.4690	89.10	88.58	71.16, 71.30	11.11, 11.20	5.15 5.20	12.16 12.43	71.42	11.28	4.90	12.40
IX	$CH_3CH{=}CHCH(CH_3)C(Cl){=}CHCH_2NHC_4H_9$	135—136	0.9174	1.4726	70.23	69.77	67.60, 67.73	10.30, 10.39	6.04 6.65	15.27 15.80	67.94	10.53	6.10	15.43
X	$CH_3CH{=}CHCH(CH_3)CH{=}CHCHN(C_2H_5)_2$ CH_3	103—104	0.8095	1.4550	70.17	69.86	80.16, 80.41	12.98, 12.99	6.51 6.79	— —	80.31	13.00	6.69	—
XI	$CH_3CH{=}CHCH(CH_3)CH{=}CHCHN(C_4H_9)_2$ CH_3	144—145	0.8141	1.4578	88.95	88.33	81.96, 82.01	13.27, 13.29	5.31 5.34	— —	81.43	13.29	5.28	—
XII	$CH_3CH{=}CHCH(CH_3)CH{=}CHCHNHC_4H_9$ CH_3	116—117	0.8065	1.4550	70.44	69.52	79.82, 80.07	12.96, 13.03	6.77 6.88	— —	80.31	13.00	6.69	—

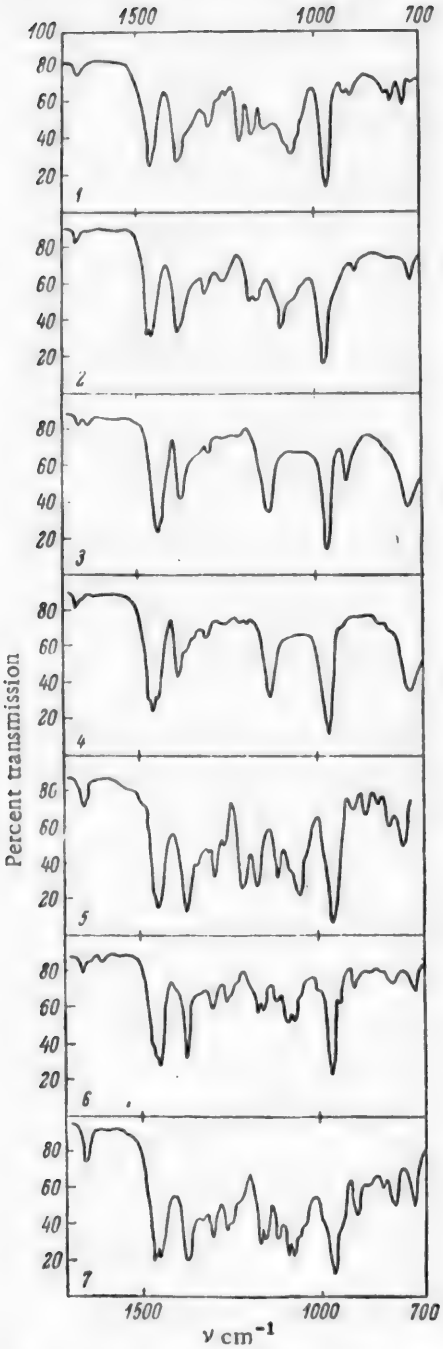


Fig. 1. Infrared transmission spectra. 1) 1-Diethylamino-5-methyl-2,6-octadiene; 2) 1-dibutylamino-5-methyl-2,6-octadiene; 3) 1-butylamino-5-methyl-2,6-octadiene (from 3-chloro-5-methyl-1,6-octadiene with a considerable admixture of 3-butylamino-5-methyl-1,6-octadiene); 4) 1-butylamino-5-methyl-2,6-octadiene (from 1-chloro-5-methyl-2,6-octadiene); 5) 1-diethylamino-3,5-dimethyl-2,6-octadiene; 6) 1-dibutylamino-3,5-dimethyl-2,6-octadiene; 7) 1-butylamino-3,5-dimethyl-2,6-octadiene.

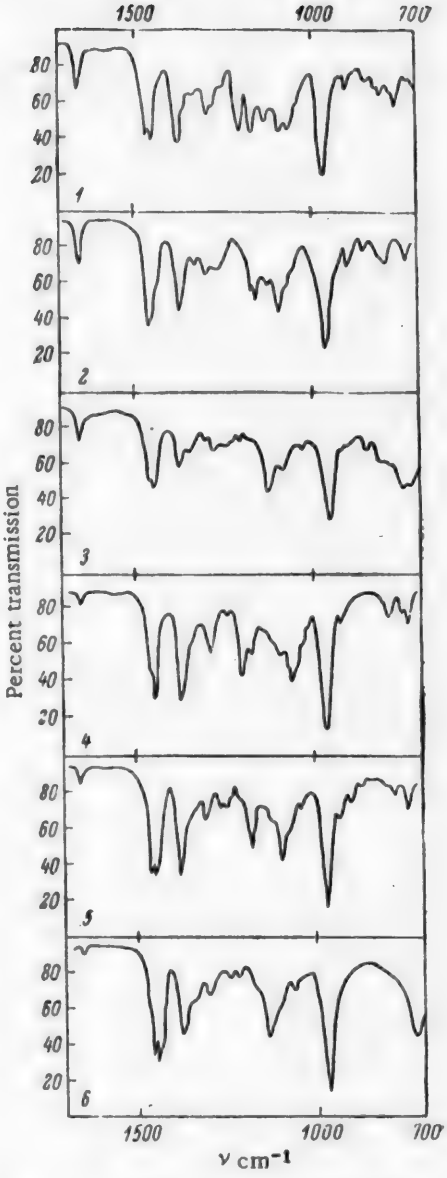


Fig. 2. Infrared transmission spectra. 1) 1-Diethylamino-3-chloro-5-methyl-2,6-octadiene; 2) 1-dibutylamino-3-chloro-5-methyl-2,6-octadiene; 3) 1-butylamino-3-chloro-5-methyl-2,6-octadiene; 4) 2-diethylamino-5-methyl-3,7-octadiene; 5) 2-dibutylamino-5-methyl-3,7-octadiene; 6) 2-butylamino-5-methyl-3,7-octadiene.

Thus, it was established that in the reaction with primary amines in some cases exchange can go without the allyl rearrangement.

EXPERIMENTAL

The methods of preparation and constants of the telomers were described in the previous work [1]. In the present work, we have used the following chlorides: 3-chloro-5-methyl-1,6-octadiene; 1-chloro-5-methyl-2,6-octadiene; 1-chloro-3,5-dimethyl-2,6-octadiene; 2-chloro-6-methyl-3,7-nonadiene; and 1,3-dichloro-5-methyl-2,6-octadiene.

A mixture of telomer (0.1 mole) and amine (50% excess in the case of secondary amines and fourfold excess for butylamine) was boiled with stirring on a water bath for ten hours in the case of the primary chlorides and 20 hours in the case of the secondary chlorides. In the reaction with secondary amines we found precipitation of a voluminous precipitate. After addition to the reaction mixture of 100 ml of 1:1 hydrochloric acid with stirring and cooling, it was extracted with ether (three times with 30 ml). The water solution was treated with solid alkali, which was added in small portions with cooling. The precipitated amine was separated and the solution was treated with ether. The ether extracts were added to the amine and dried over alkali. After distillation of the ether the amine was distilled in a vacuum. The yields of amines varied within the limits 50-70%.

The combined ether extracts which contained the unreacted chlorides were dried over calcium chloride and after distillation of the ether the content of unreacted telomer in them was determined. In the residue from amination of the telomers of divinyl (I and II) we usually found about 25% of the taken amount of chloride which had not reacted and which had a stable chlorine atom, for which we previously had shown a cyclic structure. B. p. 71-73° (10 mm), d^{20}_4 0.9717, $n^{20}D$ 1.4778.

Analytical data for the resulting amines are given in the table.

The mixture of amines obtained from butylamine and telomer (I) had the constants: b. p. 114-121° (10 mm), d^{20}_4 0.8139, $n^{20}D$ 1.4572.

The infrared spectra of the amines was photographed with a two beam IKS-14 spectrophotometer with a prism of NaCl with a layer thickness 0.032 mm. The data are given in Figs. 1 and 2.

SUMMARY

1. We have studied the reaction with primary and secondary amines of lower telomers of 2-chloro-3-pentene with diene hydrocarbons: divinyl, isoprene, piperylene, and chloroprene.

2. We have shown that with secondary amines the reaction occurs independently of the structure of the initial chloride with formation of amines of the crotyl type. The reaction with primary amines in some cases occurs with formation of both allyl isomers.

3. We have isolated and characterized 12 amines of the series $C_nH_{2n-1}N$.

LITERATURE CITED

1. A. A. Petrov, N. A. Razumova, and M. L. Genusov, Zhur. Obshch. Khim. 28, 1128, 2132, 3220 (1958);° NDVSh, Khim. 1, 530 (1958); 2, 122 (1959).
2. R. H. De Wolfe and W. G. Young, Chem. Revs. 56, 753 (1956).

°Original Russian pagination. See C. B. translation.

EXCHANGE REACTIONS OF CHLORINE-CONTAINING TELOMERS OF DIENE HYDROCARBONS

II. REACTION OF 1-CHLORO-5-METHYL-, 1-CHLORO-3,5-DIMETHYL-, AND 1,3-DICHLORO-5-METHYL-2,6-OCTADIENE WITH SODIUM ACETOACETIC ESTER

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In previous work in which one of us participated there was a description of the exchange reaction between the initial products of telomerization of divinyl, isoprene, piperylene, and chloroprene with 2-chloro-3-pentene (piperylene hydrochloride) and aliphatic amines [1]. In all cases the reaction occurred with formation of diene amines, chiefly of the crotyl type. In this communication, we describe the exchange reaction of three of the above-mentioned telomers with sodium acetoacetic ester. These reactions are of interest as intermediate steps in the synthesis of alcohols of the sesquiterpene series, their homologs and analogs.

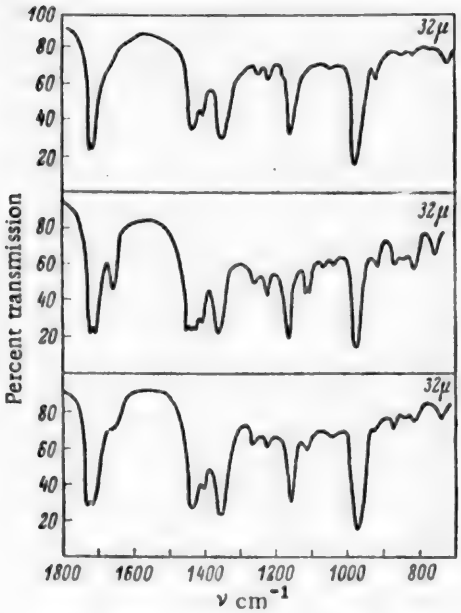
The literature describes numerous reactions of halogen derivatives with sodium acetoacetic ester. Of interest for this work are those in which crotyl chloride, prenyl chloride, and 1,3-dichloro-2-butene take part. These chlorides contain the same terminal grouping of atoms as do the telomers which we study. All these chlorides give as final products ketones which do not contain a vinyl group [2-7]; in particular, from prenyl chloride, 2-methyl-2-hepten-6-one is obtained in this way [2, 5].

TABLE 1

Substance no.	Substance	B.p. (pressure 10 mm)	d_4^{20}	n_D^{20}	MR found	MR calc.
(I)	$CH_3CH{=}CHCH(CH_3)CH{=}CHCH_2CH_2COCH_3$	109—110°	0.8672	1.4604	56.98	56.69
(II)	$CH_3CH{=}CHCH(CH_3)CCl{=}CHCH_2CH_2COCH_3$	130—131	0.9730	1.4742	62.04	61.56
(III)	$CH_3CH{=}CHCH(CH_3)C(CH_3){=}CHCH_2CH_2COCH_3$	119—120	0.8621	1.4626	62.03	61.31

Our experiments on the reaction with sodium acetoacetic ester of 1-chloro-5-methyl-, 1-chloro-3,5-dimethyl-, and 1,3-dichloro-5-methyl-2,6-octadiene (telomers of 2-chloro-3-pentene with divinyl, isoprene, and chloroprene, respectively) showed that in this case, as final products there were also obtained ketones which did not contain vinyl groups, and which had the formulas given in Table 1. The conclusion as to such structures

for the substances which we prepared was made on the basis of study of their infrared spectra. In these, we observed only frequencies for the grouping $-CH=CH-$ or $-CCl=CH-$ (970 cm^{-1} or about 840 cm^{-1}) and did not find the characteristic frequencies of the vinyl group. Thus, isomeric ketones of the type $CH_2=CH-CR_2-CH_2-CO-CH_3$, whose formation could be expected if an allylic rearrangement occurred, were absent from the reaction product.



Infrared transmission spectra. 1) 4-Methyl-2,6-undecadien-10-one; 2) 6-chloro-4-methyl-2,6-undecadien-10-one; 3) 4,6-dimethyl-2,6-undecadien-10-one.

In one of the experiments, we used a mixture of allyl isomers for the synthesis: 1-chloro-5-methyl-2,6-octadiene and 3-chloro-5-methyl-1,6-octadiene, and we obtained only a ketone which corresponded to the structure of the first substance. Hence, the reaction takes place with the more stable form of intermediate carbonium ion independent of the structure of the allyl isomer used in the reaction.

The ketones which we obtained are colorless oils with characteristic pleasant odors, insoluble in water. Their constants are given in Table 1.

The data of Table 1 show that in all these ketones the observed molecular refraction is somewhat higher than calculated.

We did not succeed in obtaining well crystallized hydrazine derivatives (semicarbazones and 2,4-dinitrophenylhydrazones) from these ketones. However, the presence of carbonyl groups is indicated perfectly clearly by their infrared spectra: they all have an intense band in the region 1705-1725 cm^{-1}, the band at about 1160 cm^{-1} which is characteristic for methyl ketones, and also an intense ketone frequency at 1360 cm^{-1}. Only in the case of ketone (II) is there a double bond which corresponds to the well-differentiated band at 1660 cm^{-1}. The bands of the double bonds in the spectra of the other two ketones appear only as projections on the intense absorption bands of the carbonyl group (figure).

These substances react well with the Grignard reagent and the Iotsich reagent. One of the following papers will be devoted to a description of these reactions.

EXPERIMENTAL

The methods of preparation and constants of the chlorides used in this study were given earlier [8]. Their reaction with sodium acetoacetic ester was carried out under the following conditions.

TABLE 2

Substance	Found, %			Calculated, %		
	C	H	Cl	C	H	Cl
(I)	79.99, 79.92	11.08, 11.37	—	79.94	11.18	—
(II)	67.00, 66.96	9.11, 8.97	16.37, 16.66	67.12	8.92	16.51
(III)	80.31, 80.33	11.36, 11.40	—	80.36	11.41	—

We added 0.25 mole of telomer by drops to sodium acetoacetic ester prepared from 4.5 g of sodium and 24 g of acetoacetic ester in 100 ml of anhydrous alcohol. The mixture was stirred for 3-4 hours with heating on a water bath to 60-70°.

On the next day, the precipitate of sodium chloride was separated by centrifuging and the alcohol was distilled from the reaction mixture in a vacuum. To the residue was added 150 ml of 10% sodium hydroxide solution and the mixture was stirred for 4-5 hours at 60-70°. After acidification to an acid reaction to Congo the reaction products were extracted with ether. The ether solution was washed with a solution of sodium bicarbonate and with water and dried over magnesium sulfate, then distilled, first at ordinary pressure (removing the ether) and then in a vacuum. The yield of ketones was on the order of 30%. In all cases we obtained considerable amounts of high boiling products which were not further investigated.

TABLE 3

Infrared Spectra of Ketones (Prism of NaCl, thickness of layer 0.032 mm)

Substance			Substance		
(I)	(II)	(III)	(I)	(II)	(III)
718 сл •	749 сл	735 сл	1223 сл	1223 ср	1223 сл
820 сл	805 сл	812 сл	1250 о. сл	1260 сл	1262 сл
845 о. сл	862 сл	867 сл	1357 с	1364 о. с	1355 о. с
918 сл	910 сл	919 о. сл	1409 сл	1409 с	1407 сл
972 о. с	973 о. с	967 о. с	—	1427 с	—
1037 о. сл	1037 сл	1035 о. сл	1438 с	1442 с	1442 с
—	1065 сл	—	—	1452 с	—
—	1103 ср	—	1660 сл	1660 ср	1660 сл
—	1118 ср	1116 сл	1715 о. с	1705 о. с	1716 о. с
1162 с	1160 с	1154 с	1720 о. с	1720 о. с	1727 о. с

• сл = weak, о. сл = very weak, ср = medium, с = strong, о. с = very strong.

The analytical data are given in Table 2. The infrared spectra are given in Table 3 and in the figure.

SUMMARY

1. We have studied the reaction of some initial telomers of diene hydrocarbons and 2-chloro-3-pentene with sodium acetoacetic ester.

2. We have showed that in all cases exchange occurs with formation of only one type of ketone which does not contain the vinyl group.

3. We have described three ketones: 4-methyl-2,6-undecadien-10-one, 4,6-dimethyl-2,6-undecadien-10-one, and 6-chloro-4-methyl-2,6-undecadien-10-one.

LITERATURE CITED

1. A. A. Petrov, N. A. Razumova, M. L. Genusov, and T. V. Yakovleva, Zhur. Obshch. Khim. 30, 1160 (1960).•
2. I. N. Nazarov, L. A. Yanovskaya, B. P. Gusev, S. S. Yufit, V. I. Gunar, and V. A. Smit, Doklady Akad. Nauk SSSR 114, 331 (1957).•
3. I. N. Nazarov, S. M. Makin, V. B. Mochalin, D. V. Nazarova, V. P. Vinogradov, B. K. Kruptsov, I. I. Nazarova, and O. A. Shavrigina, Doklady Akad. Nauk SSSR 114, 1242 (1957).•

• Original Russian pagination. See C. B. translation.

4. L. Ruzicka and H. Schinz, Helv. Chem. Acta 23, 964 (1940).
5. J. F. Arens and D. A. Van Dorp, Rec. Trav. Chim. 67, 973 (1948).
6. G. V. Isagulyants, Zhur. Priklad. Khim. 19, 35 (1946).
7. M. O. Melikyan and G. T. Tatevosyan, Zhur. Obshch. Khim. 21, 696 (1951).*
8. A. A. Petrov, N. A. Razumova, and M. L. Genusov, Zhur. Obshch. Khim. 28, 1128, 2132 (1958); NDVSh 1, 530 (1958).

* Original Russian pagination. See C. B. translation.

THE SYNTHESIS OF ANALOGS OF GERANIOL, FARNESOL, GERANYLGERANIOL, ISOPHYTOL, AND PHYTOL

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In recent years in our laboratory we have worked out practical methods for preparing important examples of isoprene compounds and their synthetic analogs. By successive repeated reactions of ethynylation, selective hydrogenation, isomerization, and acetonylation, we have obtained methylheptenone, linalool, geranylacetone, nerolidol, geranyllinalool, and various analogs of these compounds [1-7].

The present work is devoted to a study of the synthesis chiefly of primary alcohols, analogs of geraniol (IV), farnesol (XI), geranylgeraniol (XVIII), isophytol (XXVII), phytol (XXV) and intermediate compounds.

Geraniol and farnesol are valuable perfumes, long used in the perfume industry. Their analogs are of interest for a study of the relation of odor to structure. The analogs of geranylgeraniol, phytol, and isophytol are of great interest for the synthesis of the corresponding analogs of vitamins K, E (tocopherol), terpenes, and other biologically important compounds.

The synthesis of isoprene alcohols was carried out by two methods, shown in Figs. 1 and 2.

According to the first method (Fig. 1) the ketones (I, VIII, XV, XXII) were reacted with ethoxyacetylene magnesium bromide [8]. The resulting ethoxyacetylene carbinols (II, IX, XVI, XXIII) without preliminary distillation were treated in ether solution with 10% sulfuric acid. As a result of the reaction we obtained esters of α,β-unsaturated acids (III, X, XVII, XXIV) (Table 1). Reduction of the esters of the α,β-unsaturated acids with lithium aluminum hydride gave good yields of primary alcohols, the analogs of geraniol (IV), farnesol (XI), geranylgeraniol (XVIII), and phytol (XXV). The primary alcohols obtained by these methods are shown in Table 2.

The synthesis of primary alcohols by the second method (Figs. 1 and 2) was carried out by us from tertiary ethylenic alcohols, analogs of linalool (VI) [4], nerolidol (XIII), and geranyllinalool (XX) [7].

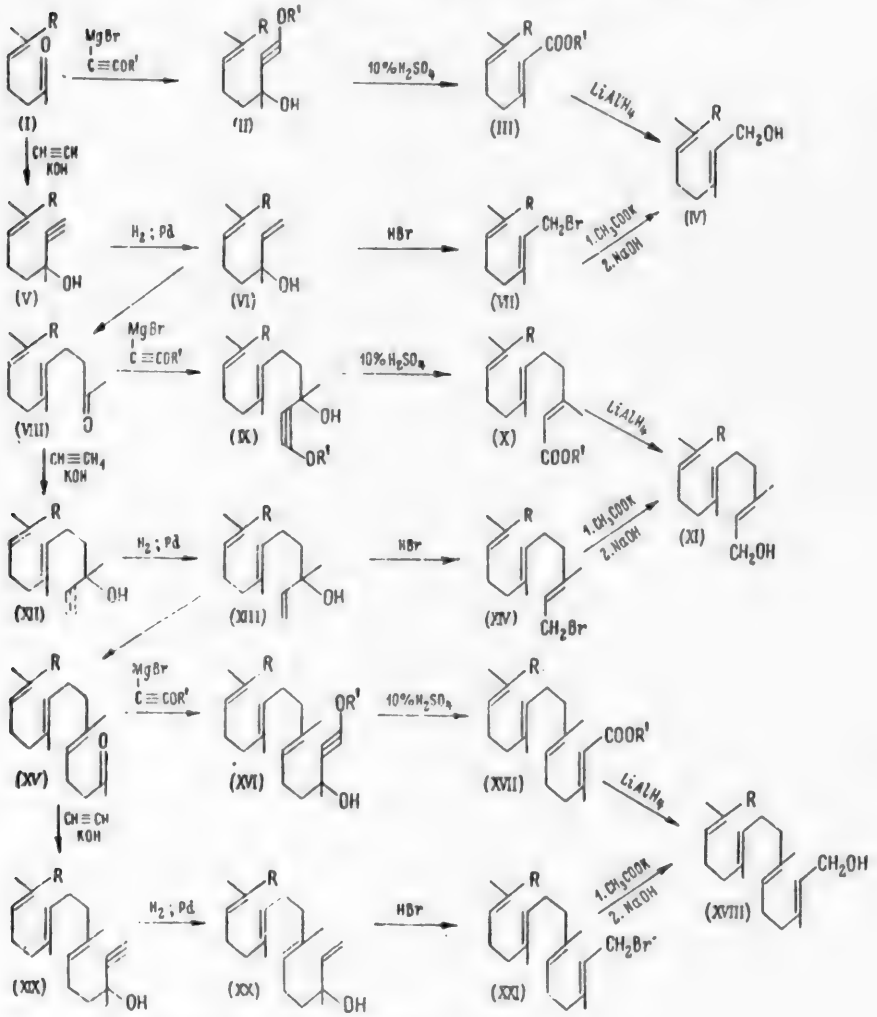
In the action of hydrogen bromide on these tertiary ethylenic alcohols in isooctane solution we obtained primary allyl bromides which by reaction with potassium acetate in dimethylformamide solution and later saponification of the resulting acetates by 10% alkali were easily converted into primary alcohols, analogs of geraniol (IV), farnesol (XI), and geranylgeraniol (XVIII).

All the processes of isomerization of tertiary alcohols into primary ones were carried out without separating the intermediate products and in one step.

All the primary alcohols obtained by us by this method were chromatographed on a column filled with aluminum oxide for purification and also for separation of possible isomers. However, in all cases, the primary alcohol was obtained in only one stereoisomeric form. Evidently, the isomerization reaction is stereospecific.

Scheme 1

Synthesis of Analogs of Geraniol, Farnesol, and Geranylgeraniol



Scheme 2

Synthesis of Analogs of Phytol and Isophytol

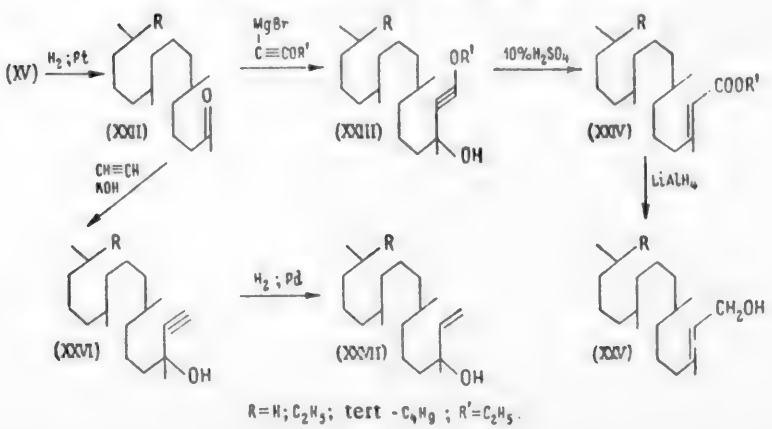


TABLE 1

Ethyl Esters of α, β-Unsaturated Acids, Obtained through Ethoxyacetylene

α, β-Unsaturated ester (R = C_2H_5)	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Found, %		Calc., %		Yield (in %)
				found	calc.	C	H	C	H	
(III) R = H	63—65° (0.5)	1.4620	0.9147	54.76	53.72	72.43, 72.61	9.86, 10.04	72.44	9.94	65
(III) R = tert-C_4H_9	89—92 (0.1)	1.4683	—	—	—	—	—	—	—	71
(X) R = H	105—107 (0.3)	1.4791	0.9168	77.47	76.42	76.66, 76.54	10.55, 10.37	76.75	10.46	75
(X) R = tert-C_4H_9	118—120 (0.02)	1.4797	0.9088	95.32	94.24	78.69, 78.61	11.19, 11.23	78.43	11.11	70
(XVII) R = tert-C_4H_9	151—154 (0.01)	1.4870	0.9078	118.40	117.43	80.36, 80.51	11.30, 11.19	80.21	11.23	75
(XXIV) R = H	152—155 (0.5)	1.4586	0.8732	101.41	100.36	77.48, 77.46	12.49, 12.30	77.71	12.42	79
(XXIV) R = C_2H_5	137—140 (0.011)	1.4598	0.8730	110.60	109.55	78.52, 78.66	12.32, 12.35	78.34	12.58	63.5
(XXIV) R = tert-C_4H_9	147—150 (0.02)	1.4650	0.8792	119.70	118.83	79.27, 78.96	12.54, 12.49	78.88	12.71	70

TABLE 2

Primary Alcohols

Primary alcohol	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found, % C	Found, % H	Calc., % C	Calc., % H	Yield (in %) meth. A •	Yield (in %) meth. B ••	Diphenylurethane m.p.	Diphenylurethane % N found	Diphenylurethane % N calc.
(IV) R = H	56—58° (0.25)	1.4696	0.8770	44.53	44.35	76.81, 76.87	11.42, 11.62	77.09	11.52	90	—	102—104° •••	4.30, 4.50	4.20
(IV) R = C_2H_5	86—88 (2)	1.4751	0.8810	53.78	53.75	78.71, 78.84	11.90, 12.08	78.53	11.98	—	45	46—47	4.09, 4.17	3.85
(IV) R = iso -C_3H_7	91—92 (2)	1.4740	0.8795	58.22	58.27	79.40, 79.23	12.15, 11.98	79.12	12.09	—	50	79—80	3.87, 3.83	3.71
(IV) R = tert -C_4H_9	86—87 (0.02)	1.4750	0.8832	62.50	62.81	79.67, 79.76	12.06, 11.96	79.59	12.24	81	62	80.5—81	3.83, 3.81	3.57
(XI) R = H	105—108 (0.16)	1.4841	0.8954	66.71	66.94	79.81, 79.92	11.33, 11.26	80.21	11.51	80	—	—	—	—
(XI) R = C_2H_5	95—96 (0.03)	1.4851	0.8878	76.32	76.20	81.58, 81.55	11.84, 12.00	81.29	11.94	—	60	—	—	—
(XI) R = tert-C_4H_9	134—136 (0.03)	1.4868	0.8906	85.27	85.44	81.46, 81.49	12.09, 12.21	81.75	12.19	80	59	—	—	—
(XVIII) R = C_2H_5	145—147 (0.02)	1.4900	0.8911	98.79	98.84	82.75, 82.91	11.69, 11.78	82.82	11.92	—	60	—	—	—
(XVIII) R = tert-C_4H_9	157—159 (0.03)	1.4912	0.8972	108.07	107.80	83.03, 82.90	12.08, 11.93	83.13	12.05	81	59	—	—	—
(XXV) R = H	144—146 (0.16)	1.4658	0.8561	91.16	91.00	81.28, 81.49	13.30, 13.21	80.77	13.55	90	—	—	—	—
(XXV) R = C_2H_5	142—144 (0.06)	1.4667	0.8586	100.32	100.19	81.11, 81.00	13.86, 13.66	81.19	13.65	80.5	—	—	—	—
(XXV) R = tert -C_4H_9	161—164 (0.07)	1.4692	0.8628	109.30	109.47	82.04, 81.85	13.60, 13.75	81.58	13.69	75	—	—	—	—

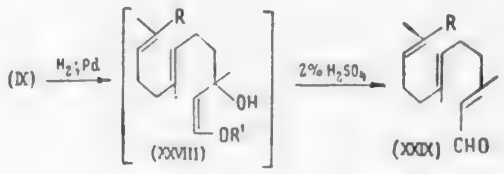
• Method A — obtaining primary alcohols by reduction of α, β-unsaturated esters with $LiAlH_4$.

•• Method B — obtaining primary alcohols by isomerization of tertiary vinylcarbinols.

••• The data refer to the 3-nitrophthalate.

The constants of the alcohols obtained by this method agree very well with the constants of the alcohols obtained by reduction of the esters of α,β-unsaturated acids with lithium aluminum hydride. The primary alcohols obtained by both methods are shown in Table 2.

In the present work we were also interested in converting ethoxyethynyl carbinols (IX) into the corresponding unsaturated aldehydes, analogs of farnesal (XXIX). This conversion was studied in the example of compound (IX, R = tert-C_4H_9).



In an attempt to distill the ethoxyacetylenic carbinol (IX, R = tert-C_4H_9) in a high vacuum (0.01 mm) we found a spontaneous decomposition of the substance when heated above 100°. Therefore, the carbinol (IX) was selectively hydrogenated in the impure form and the content of pure carbinol in the substance was estimated by the amount of active hydrogen (Chugaev-Tserevitinov reaction). The ethoxyethylenic carbinol (XXVIII, R = = tert-C_4H_9) without preliminary distillation was treated with 2% sulfuric acid and we obtained in 70% yield the analog of farnesal (XXIX, R = tert-C_4H_9) as a mixture of isomers. The individual isomers could be separated as 2,4-dinitrophenylhydrazones by fractional crystallization.

EXPERIMENTAL

Hydrogenation of the analog of farnesylacetone (XV) to a saturated ketone (XXII).

a) 6,10-Dimethylpentadecan-14-one (XXII, R = H). Thirty g of 6,10-dimethylpentadecan-2,6,10-trien-14-one (XV, R = H) in 45 ml of methanol was exhaustively hydrogenated (9000 ml, 19°, 740 mm) in the presence of a Pt catalyst. At the end of hydrogenation, the catalyst was filtered off, the methanol was removed in a weak vacuum, and the product was distilled. We obtained 24.4 g (81.7%) (XXII, R = H).

B. p. 94-96° (0.02 mm), $n^{20}D$ 1.4450, d^{20}_4 0.8434; MR_D 80.30; calc. 80.71.

Found %: C 80.52, 80.56; H 13.34, 13.31. $C_{17}H_{34}O$. Calculated %: C 80.31; H 13.42.

2,4-Dinitrophenylhydrazone has m. p. 33-34°.

Found %: N 13.24, 13.20. $C_{23}H_{38}O_4N_4$. Calculated %: N 12.89.

In an analogous way we obtained the following substances.

b) 3,7,11-Trimethylhexadecan-15-one (XXII, R = C_2H_5) in a yield of 90%.

B. p. 128-130° (0.06 mm), $n^{20}D$ 1.4480, d^{20}_4 0.8391, MR_D 90.12; calc. 89.93.

Found %: C 80.99, 80.94; H 13.44, 13.49. $C_{19}H_{38}O$. Calculated %: C 80.78; H 13.56.

Semicarbazone m. p. 62-63°.

Found %: N 12.66, 12.53. $C_{20}H_{41}O_3N_3$. Calculated %: N 12.38.

c) 2,2,3,7,11-Pentamethylhexadecan-15-one (XXII, R = tert-C_4H_9) with a yield of 83.7%.

B. p. 126-128° (0.02 mm), $n^{20}D$ 1.4558, d^{20}_4 0.8511, MR_D 99.15; calc. 99.18.

Found %: C 81.20, 80.88; H 13.16, 13.38. $C_{21}H_{42}O$. Calculated %: C 81.21; H 13.68.

2,4-Dinitrophenylhydrazone m. p. 31-32°.

Found %: N 11.59, 11.62. $C_{27}H_{46}O_4N_4$. Calculated %: N 11.42.

Condensation of Ketones with Ethoxyethynyl Magnesium Bromide

8-Ethoxy-6-methyl-2-octen-7-yn-6-ol (II, R = H). To an ether solution of ethyl magnesium bromide obtained from 9.7 g of magnesium, 52 g of ethyl bromide, and 150 ml of absolute ether, we added during one hour with stirring at room temperature 30 g of ethoxyacetylene in 60 ml of dry ether. The mixture was stirred for 15 minutes more at 35° until evolution of ethane stopped. After cooling the mixture with ice and salt we added in the course of one hour 40 g of 2-hepten-6-one (I, R = H), after which the reaction mixture was stirred for one hour at room temperature and 30 minutes at 35°. The resulting alcoholate was decomposed with 250 ml of 20% ammonium chloride solution. The ether layer was separated and the water was extracted with ether. The combined ether solutions were washed with water and dried over magnesium sulfate. After distillation, we obtained 46.8 g (65%) of (II, R = H).

B. p. 69-72° (0.085 mm), $n^{20}D$ 1.4634, d^{20}_4 0.9281, MR_D 54.04; calc. 53.70.

Found %: C 72.15, 72.19; H 9.92, 9.89. $C_{11}H_{18}O_2$. Calculated %: C 72.44; H 9.94.

Synthesis of Esters of α,β-Unsaturated Acids (III, X, XVII, XXIV)

Using Ethoxyacetylene

Ethyl ester of 2,2,3,7,11-pentamethyltridecan-3,7,11-trien-13-oic acid (X, R = tert-C_4H_9, R' = C_2H_5). To ethyl magnesium bromide obtained from 3.12 g of magnesium and 16 g of ethyl bromide in 60 ml of anhydrous ether with stirring was added dropwise over the course of one hour 9.2 g of ethoxyacetylene in 40 ml of anhydrous ether, and the mixture was heated for 30 minutes at 35°. After the mixture had been cooled with ice and salt, in an atmosphere of nitrogen during one hour was added 23.6 g of 2,2,3,7-tetramethyldodeca-3,7-dien-11-one (VIII, R = tert-C_4H_9). The reaction mass was stirred for 1.5 hours at room temperature and 0.5 hour at 35°. The mixture was cooled to room temperature and with energetic stirring 320 ml of 10% sulfuric acid was added, after which stirring was continued for two hours more. The ether layer was separated, washed with water, to a neutral reaction to litmus, and dried over magnesium sulfate. After distillation of the ether the product was distilled in a high vacuum. We obtained 21.3 g (X, R = tert-C_4H_9, R' = C_2H_5). In an analogous way we also obtained the other ethyl esters of α,β-unsaturated acids shown in Table 1.

2,2,3,7-Tetramethylnona-3,7-dien-9-oic acid (III, R = tert-C_4H_9, R' = H). To a solution of 7.14 g of the ethyl ester of 2,2,3,7-tetramethylnona-3,7-dien-9-oic acid (III, R = tert-C_4H_9, R' = C_2H_5) heated to boiling in 5 ml of methyl alcohol we added 1.3 g of sodium hydroxide in 15 ml of water. The mixture was heated to boiling in a stream of nitrogen for two hours, cooled, and acidified with 10% sulfuric acid to an acid reaction. The oily layer was separated, the water was extracted with ether and the combined ether extracts and oily layer were dried with magnesium sulfate. After distillation, we obtained 4.4 g (33%) of (III, R = tert-C_4H_9, R' = H).

B. p. 119-120° (0.04 mm), $n^{20}D$ 1.4820, d^{20}_4 0.9400, MR_D 63.70; calc. 62.83.

Found %: C 74.57, 74.54; H 10.53, 10.36. $C_{13}H_{22}O_2$. Calculated %: C 74.28; H 10.47.

2,2,3,7,11-Pentamethyltrideca-3,7,11-trien-13-al (XXIX, R = tert-C_4H_9). To ethoxyacetylene magnesium bromide prepared from 1.56 g of magnesium, 8 g of ethyl bromide and 4.6 g of ethoxyacetylene in 60 ml of absolute ether was added 11.8 g of 2,2,3,7-tetramethyldodeca-3,7-dien-11-one (VIII, R = tert-C_4H_9) with cooling with ice and salt, in a stream of nitrogen in the course of one hour. The reaction mass was stirred for one hour at room temperature and 30 minutes at 35°, then with ice cooling was treated with 100 ml of 20% ammonium chloride solution. The ether layer was separated and the water was extracted with three portions of ether. The combined ether extracts were dried with ignited potash. The ether was distilled off in a vacuum and 13.8 g of substance was obtained. By the Chugaev-Tserevitinov method it was found that the substance contained 90% of the alcohol (IX, R = tert-C_4H_9, R' = C_2H_5). Eleven g of this alcohol was selectively hydrolyzed over $Pd/CaCO_3$ catalyst. After the theoretically calculated amount of hydrogen (835 ml, 24°, 749 mm) had been absorbed, hydrogenation was stopped. The catalyst was filtered off, then 75 ml of 3% sulfuric acid was added to the ether solution, and the mixture was stirred energetically for 2 hours at room temperature. The ether layer was separated, washed with a solution of sodium bicarbonate and dried over magnesium sulfate. After distillation in a vacuum, we obtained 5.7 g (70%) of (XXIX, R = tert-C_4H_9).

B. p. 124-126° (0.02 mm), $n^{20}D$ 1.4870, d^{20}_4 0.8892, MR_D 84.73; calc. 83.92.

Found %: C 82.44, 82.29; H 11.24, 11.21. $C_{18}H_{30}O$. Calculated %: C 82.44; H 11.45.

The 2,4-dinitrophenylhydrazone of this aldehyde (XXIX) was separated into two isomers by fractional crystallization.

First isomer, m. p. 99.5-101°.

Found %: N 12.64, 12.53. $C_{24}H_{34}O_4N_4$. Calculated %: N 12.67.

Second isomer, m. p. 133.5-135°.

Found %: N 12.89, 12.86. $C_{24}H_{34}O_4N_4$. Calculated %: N 12.67.

Synthesis of Primary Alcohols (IV, XI, XVIII, XXV) by Reduction of Esters of α,β-Unsaturated Acids by Lithium Aluminum Hydride

Method A

6-Methylocta-2,6-dien-8-ol (IV, R = H). In a three-necked flask fitted with a mechanical stirrer, reflux water condenser, and dropping funnel with a drying tube was placed 120 ml of an ether solution of lithium aluminum hydride (concentration 0.0635 mg/ml). At − 65° was added dropwise 21 g of the ethyl ester of 6-methylocta-2,6-dien-8-oic acid (III, R = H, R' = C_2H_5) in 100 ml of absolute ether and then the mixture was stirred one hour at −30°. The temperature of the mixture was raised to that of the room and excess lithium aluminum hydride was decomposed by the addition of 35 ml of ethyl acetate. The resulting thick mass was dissolved by addition of 100 ml of a saturated solution of ammonium chloride. The solution was filtered from the precipitate which formed. The ether layer was separated, washed with water, and dried over anhydrous magnesium sulfate. After distillation of the ether the residue was distilled in a vacuum. We obtained 14.5 g of (IV, R = H).

In an analogous way, we obtained the other primary alcohols described in Table 2.

Reduction of ester (XXIV) to the corresponding analog of phytol (XXV) was better carried out at room temperature.

Synthesis of Primary Alcohols (IV, XI, XVIII) by Isomerization of Tertiary Vinyl Carbinols (VI, XIII, XX)

Method B

2,2,3,7-Tetramethylnona-3,7-dien-9-ol (IV, R = tert-C_4H_9). Ninety-eight g of 2,2,3,7-tetramethylnona-3,8-dien-7-ol (VI, R = tert-C_4H_9) was saturated with 42.5 g of hydrogen bromide while cooled with ice and salt and the reaction mixture was allowed to stand overnight. The reaction product was diluted with ether (150 ml), the water layer which separated was removed, and the ether solution of bromide was washed with 5% sodium bicarbonate solution and dried with sodium sulfate. The ether was distilled off and the resulting bromide was added in the course of 15 minutes to a solution of 52.5 g of potassium acetate in 500 ml of dimethylformamide and the mixture was stirred for one hour at room temperature and then for two hours at 60°. The precipitate was filtered off and washed with ether. The dimethylformamide was distilled in a weak vacuum and the acetate was washed with water to remove traces of dimethylformamide. Saponification of the acetate was carried out by heating it with 40 g of sodium hydroxide in 400 ml of water for five hours at 70°. The oily layer was separated and the water was extracted with ether. The combined ether extracts and oily layer were saturated with carbon dioxide gas and dried with magnesium sulfate. After distillation of the ether the residue was distilled in a vacuum. We obtained 60.8 g of (IV, R = tert-C_4H_9).

In an analogous way, we also obtained the other primary alcohols shown in Table 2.

Synthesis of Analogs of Isophytol

2,2,3,7,11,15-Hexamethylheptadec-16-yn-15-ol (XXVI, R = tert-C_4H_9). In a 1.5 liter steel reactor was placed 700 ml of absolute ether, 30 g of powdered potassium hydroxide, and with energetic stirring, the mixture was saturated with acetylene at − 8° and a pressure of 9 atm, which was maintained for the duration

of the reaction. After 40 minutes we added to the reactor 20 g of ketone (XXII, R = tert-C_4H_9), and then stirring of the reaction mass was continued for 2.5 hours more. The temperature at the end of the experiment slowly rose to 20°. Then the acetylene pressure was lowered and 0.5 liter of water was added to the mixture. The ether layer was separated and the water was extracted with ether. The combined ether extracts were neutralized with carbon dioxide gas and dried with magnesium sulfate. The ether was distilled and after distillation of the residue in a vacuum we obtained 17.3 g (80%) of (XXVI, R = tert-C_4H_9).

B. p. 138-141° (0.03 mm), $n^{20}D$ 1.4654, d^{20}_4 0.8664, MR_D 107.8; calc. 107.93.

Found %: C 82.18, 82.23; H 13.32, 13.23. $C_{23}H_{44}O$. Calculated %: C 82.07; H 13.17.

2,2,3,7,11,15-Hexamethylheptadec-16-en-15-ol (XXVII, R = tert-C_4H_9). We selectively hydrogenated 10.9 g of (XXVI, R = tert-C_4H_9) in the presence of 0.05 g of Pd/$CaCO_3$ catalyst. After absorption of the theoretical amount of hydrogen (821 ml, 19°, 736 mm) hydrogenation was stopped. The catalyst was filtered off and the product was distilled in a vacuum. We obtained 9.2 g (84%) (XXVII, R = tert-C_4H_9).

B. p. 156-159° (0.2 mm), $n^{20}D$ 1.4630, d^{20}_4 0.8519, MR_D 109.50; calc. 109.47.

Found %: C 81.60, 81.67; H 13.48, 13.45. $C_{23}H_{46}O$. Calculated %: C 81.58; H 13.69.

SUMMARY

1. By two different methods we have worked out the synthesis of primary alcohols analogous to geraniol, farnesol, geranylgeraniol, and phytol.

2. Starting from analogs of farnesylacetone we have carried out the synthesis of analogs of isophytol.

LITERATURE CITED

1. I. N. Nazarov, et al., Doklady Akad. Nauk SSSR 114, 331 (1957).*
2. I. N. Nazarov, et al., Doklady Akad. Nauk SSSR 114, 1029 (1957).*
3. I. N. Nazarov, et al., Doklady Akad. Nauk SSSR 114, 1242 (1957).*
4. I. N. Nazarov, et al., Doklady Akad. Nauk SSSR 114, 796 (1957) *
5. I. N. Nazarov, B. P. Gusev, and V. I. Gunar, Zhur. Obshch. Khim. 28, 1444 (1958).*
6. I. N. Nazarov, et al., Zhur. Obshch. Khim. 29, 744 (1959).*
7. I. N. Nazarov, et al., Zhur. Obshch. Khim. 29, 1176 (1959).*
8. I. N. Nazarov, Zh. A. Krasnaya, and V. P. Vinogradov, Zhur. Obshch. Khim. 28, 460 (1958).*

* Original Russian pagination. See C. B. translation.

SYNTHESIS AND PYROLYSIS OF ESTERS OF ALKYLARSONIC ACIDS

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Ya. F. Komissarov and co-workers showed [1] that esters of alkylarsonic acids isomerized on heating into esters of arsenious acid: $RAs(O)(OR)_2 \rightarrow As(OR)_3$. The reaction was accompanied by formation of the corresponding alcohol and a fraction in which there was more trivalent arsenic than in the esters of arsenious acid which were formed.

It seemed interesting to us to study the behavior of esters of alkylarsonic acids when heated under other conditions. The required esters of alkylarsonic acid were obtained by oxidizing the corresponding esters of alkylarsonous acids* with selenium dioxide [3, 4] in dry benzene. The synthesized esters of alkylarsonic acids (Table 1) were colorless or slightly yellow viscous liquids with a weak characteristic odor, easily hydrolyzed by water and moist air.

TABLE 1

Esters of Alkylarsonic Acids

No.	Compound	B.p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	% As found	% As calc.	Yield, %
1	$C_3H_7AsO(OC_2H_5)_2$	120.5—122.5°(10)	1.2460	1.4519	48.51	48.48	33.44	33.44	53.3
2	$C_3H_7AsO(OC_3H_7)_2$	101 —103.5 (2)	1.1739	1.4520	57.95	57.72	29.67	29.71	54.8
3	$C_3H_7AsO(OC_4H_9)_2$	115 —118 (3)	1.1324	1.4532	66.91	66.95	26.73	26.74	66.1
4	$CH_3AsO(OC_4H_9)_2$	129.5—130 (5)	1.1774	1.4532	—	—	—	—	65.2
		160.3—161.3 (13) [5]	1.1728 [5]	1.4524 [5]	—	—	—	—	—
5	$C_2H_5AsO(OC_4H_9)_2$	125 —130 (5)	1.1481	1.4537	62.75	62.34	27.68	28.15	60.0

Pyrolysis of the esters of alkylarsonic acids was carried out by heating these compounds at atmospheric pressure with distillation of the easily boiling products. Decomposition began at 200-220° in the reaction mass. For isolation of individual substances the distillate was submitted to fractional distillation.

The esters of alkylarsonic acids which were synthesized were evidently quite stable to thermal action. Thus, with energetic heating of diethyl n-propylarsonate a considerable part of it distilled without change. For more complete conversion of the other esters of alkylarsonic acids, they were heated in such a way that the

* We have earlier reported the synthesis of esters of alkylarsonous acids from alkyldiiodoarsines and the corresponding alcohols in the presence of bases [2]. The esters obtained by this process have iodine-containing admixtures, but were entirely suitable for synthesis of esters of alkylarsonic acids.

temperature of the distilling vapor did not exceed 200°. Then the chief arsenic-containing products, in distinction from the previous work [1], were the corresponding esters of alkylarsonous acids (Table 2). The structure of the latter was confirmed by the reaction with hydriodic acid: in the case of esters of alkylarsonious acid the product was a brown, oily alkyldiiodoarsine, but the esters of arsenious acid were saponified to a white, flaky precipitate of arsenious anhydride. The formation of esters of arsenious acid was found in the pyrolysis of diethyl and di-n-butyl esters of n-propylarsonic acid. In the second case, the isomerization product, from its arsenic content, was close to the propyl ester of dibutyl arsenious acid, but was distinguished from the latter [6] by the value of $n^{20}D$. Pyrolysis of the di-n-propyl ester of n-propylarsonic acid evidently led to formation of tripropyl arsenite and the dipropyl ester of propylarsonic acid, but separation of the latter was difficult because of the closeness of the boiling points.

TABLE 2

Pyrolysis of Esters of Alkylarsonic Acids

No.	Starting ester	Substances obtained	B.p. (pressure in mm)	d^{20}	n_D^{20}	Yield, %
1	$C_3H_7AsO(OC_2H_5)_2$	b) $C_3H_7AsO(OC_2H_5)_2$	121.5—124°(11)	1.2435	1.4520	40.7
		a) $C_3H_7OAs(OC_2H_5)_2$	56 — 59(10)	1.1623	1.4413	11.2
2	$C_3H_7AsO(OC_3H_7)_2$	C_3H_7OH *	—	—	—	8.4
3	$C_3H_7AsO(OC_4H_9)_2$	C_4H_9OH	115 —117.5	0.8143	1.3972	17.1
		$C_3H_7As(OC_4H_9)_2$	111 —115(12)	1.0573	1.4528	5.7
		$C_3H_7OAs(OC_4H_9)_2$ **	121 —125(11)	—	1.4486	2.1
4	$CH_3AsO(OC_4H_9)_2$	C_4H_9OH *	115.5—116	—	—	9.3
		$CH_3As(OC_4H_9)_2$	93 —95(13)	1.0846	1.4515	12.5
5	$C_2H_5AsO(OC_4H_9)_2$	C_4H_9OH *	115.5—117	—	—	15.5
		$C_2H_5As(OC_4H_9)_2$	103 —106(13)	1.0727	1.4533	19.6

* Identified as 3,5-dinitrobenzoate.

** Found %: As 26.62. $C_3H_7OAs(OC_4H_9)_2$. Calculated %: As 26.74.

In almost all the cases (Nos. 2-5, Table 2) thermal decomposition of the esters of alkylarsonic acids was accompanied by formation of an alcohol with the radical found in the alkoxy group of the original ester. In the pyrolyzate of di-n-butyl methylarsonate there was a carbonyl compound which reacted with 2,4-dinitrophenylhydrazone.

EXPERIMENTAL

Preparation of diethyl n-propylarsonate. In a flask fitted with a reflux condenser we placed 12.2 g of selenium dioxide and 400 ml of anhydrous benzene. To the solution in the flask, heated to boiling, we added 39.0 g of diethyl n-propylarsonite. The color of the reaction mixture changed to black, and metallic selenium separated. After it had been heated for three hours, the reaction mixture was cooled, the selenium was filtered off, the solvent was distilled, and the residue was twice vacuum distilled. We obtained 23.38 g (53.3%) of diethyl n-propylarsonate (Table 1, substance No. 1).

The other alkyl esters of the alkylarsonic acids were obtained by an analogous method by oxidation of the corresponding ester of the alkylarsonous acid by selenium dioxide.

Pyrolysis of diethyl n-propylarsonate. In a distillation flask fitted with thermometers to measure the temperature in the reaction mixture and the vapor we heated energetically 22.5 g of diethyl n-propylarsonate, whereupon a liquid with b. p. 235-242° distilled over (20.99 g). The residue in the flask (1.23 g) was tarry. As a result of repeated vacuum distillations, the distillate was separated into two substances:

a) 2.50 g of n-propyl diethylarsonite (Table 2, No. 1a).

Found %: As 34.09. MR_D 49.66. $C_7H_{17}O_3As$. Calculated %: As 33.44. MR_D 50.07.

b) 9.16 g of diethyl n-propylarsonite (Table 2, No. 1b).

Pyrolysis of di-n-propyl n-propylarsonate. We heated 11.17 g of the di-n-propyl ester for one hour in a distilling flask in such a way that the temperature of the distilling vapor lay between 159-174° and that of the reaction mass between 244-272°. As a result of the distillation we obtained 7.41 g of pyrolyzate and a tarry residue (3.0 g). After distillation two fractions of distillate were obtained.

The first was 0.67 g (8.4%) of a substance with b. p. 25-35° (11 mm). A colorless liquid which easily evaporated at this pressure. In the reaction [7] with 3,5-dinitrobenzoyl chloride, needle shaped crystals were formed with m. p. 70-71.5° (from ligroin). A sample mixed with n-propyl 3,5-dinitrobenzoate melted in the same range. According to the literature, m. p. 74° [8].

The second was 1.54 g of a liquid with b. p. 87-94° (11 mm), d^{20}_4 1.0849, $n^{20}D$ 1.4489.

According to the literature di-n-propyl propylarsonite [2] boils at 106-107° (35 mm), d^{20}_4 1.0829, $n^{20}D$ 1.4509; tri-n-propyl arsenite [9] boils at 94-96° (11 mm), d^{20}_4 1.1277, $n^{20}D$ 1.4427.

In the reaction of 1.03 g of the resulting liquid with 3 g of potassium iodide in 20 ml of 18% hydrochloric acid in a sulfur dioxide atmosphere there separated a white, flaky precipitate and an orange, oily liquid. The latter after drying with calcium chloride had b. p. 131° (11.5 mm). B. p. of propyldiiodoarsine [10] 133.5-137° (11 mm).

Pyrolysis of di-n-butyl n-propylarsonic acid. In the thermal decomposition of 23.32 g of the ester by a method analogous to the preceding there was formed 19.13 g of distillate with b. p. 160-180° and 7.54 g of tar. Repeated distillation of the pyrolyzate gave the following products:

n-Butyl alcohol [11] 2.55 g, and 1.52 g of di-n-butyl n-propylarsonite (Table 2, No. 3).

Found %: As 28.47. MR_D 67.52. $C_{11}H_{25}O_2As$. Calculated %: As 28.43. MR_D 67.70.

In the reaction of this ester with hydriodic acid we obtained propyldiiodoarsine with b. p. 130° (11 mm).

Pyrolysis of di-n-butyl methylarsonate. Thermal decomposition of 22.03 g of ester led to formation of 15.67 g of distillate with b. p. 167-200° and 5.15 g of tarry product. After distillation we obtained a distillate of the following fractions (Table 2, No. 4).

First, 0.42 g of a substance with b. p. 113-115°. In the reaction [7] with 2,4-dinitrophenylhydrazine it gave a yellow precipitate. We could not isolate the hydrazone in pure form.

Second, 1.20 g (9.3%) of n-butyl alcohol with b. p. 115.5-116°. In the reaction [7] with 3,5-dinitrobenzoyl chloride it gave soft, silky crystals with m. p. 61-62°. A sample mixed with n-butyl 3,5-dinitrobenzoate melted at the same temperature. According to the literature [8], m. p. 64°.

Third, 2.57 g of di-n-butyl methylarsonite.

Found %: As 31.69. MR_D 58.82. $C_9H_{21}O_2As$. Calculated %: As 31.72. MR_D 58.57.

Pyrolysis of di-n-butyl ethylarsonate. In the thermal decomposition of 21.06 g of ester there distilled 14.63 g of distillate with b. p. 157-193°; residue (5.80 g) formed a tar. Fractionation of the distillate led to separation of the following substances (Table 2, No. 5):

First, 1.82 g (15.5%) of n-butyl alcohol, characterized as the n-butyl 3,5-dinitrobenzoate [7] with m. p. 62-63°. A sample mixed with n-butyl 3,5-dinitrobenzoate gave no depression of the melting point. According to the literature [8], m. p. 64°.

Second, 3.88 g of di-n-butyl ethylarsonite.

Found %: As 29.85. MR_D 63.07. $C_{10}H_{23}O_2As$. Calculated %: As 29.94. MR_D 63.19.

SUMMARY

We have found that thermal decomposition of alkyl esters of alkylarsonic acids results in formation of two arsenic-containing products, esters of alkylarsonous acid and trialkylarsenites. The reaction is accompanied by formation of an alcohol with the radical found in the alkoxy group of the original ester of the alkylarsonic acid.

LITERATURE CITED

1. Ya. F. Komissarov, A. S. Sorokoumov, and A. Ya. Maleeva, Doklady Akad. Nauk SSSR 56, 51 (1947).
2. Gil'm Kamai and B. D. Chernokal'skii, Trudy Kazan. Khim.-Tekh. Inst. im S. M. Kirova 23, 143 (1957).
3. Ya. F. Komissarov, A. Ya. Maleeva, and A. S. Sorokoumov, Doklady Akad. Nauk SSSR 55, 729 (1947).
4. L. M. Werbel, T. P. Dawson, J. R. Hootson, and T. E. Dalbey, J. Org. Chem. 22, 452 (1957).
5. E. J. Salmi, K. Merivuori, and E. Laaksonen, Suomen Kemistilehti 19, 102 (1946); Chem. Abs. 41, 5440 (1947).
6. Gil'm Kamai and Z. L. Khisamova, Zhur. Obshch. Khim. 26, 414 (1956).*
7. S. Vaibel', Identification of Organic Compounds [Russian translation] (IL, 1957), Vol. 72, p. 107.
8. W. Bryant, J. Am. Chem. Soc. 54, 3758 (1932); Zbl. (1932), Vol. II, p. 3216.
9. K. I. Kuz'min and Gil'm Kamai, Zhur. Obshch. Khim. Sbornik 1, 228 (1953).
10. W. Steinkopf, H. Dudek, and S. Schmidt, Ber. 61, 1916 (1928).
11. Handbook of Chemistry [in Russian] (1951), Vol. 2, pp. 722, 1039.

* Original Russian pagination. See C. B. translation.

N-α-HYDROXYBENZYLARYLSULFONAMIDES

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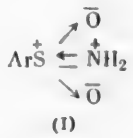
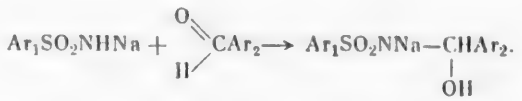
We earlier reported the preparation of N-β-hydroxyalkylarylsulfonamides by the reaction of arylsulfonamides with propylene oxide [1]. Analogous compounds have been described in [2, 3]. In the present work, we have prepared some N-α-hydroxybenzylarylsulfonamides. The reaction of arylsulfonamides (I) occurs with the splitting of two atoms of hydrogen from the benzenesulfonamide group which is probably connected with the junction of the benzene ring and the sulfonamide group, and also the electrophilic action of the sulfur atom.



(I)

This splitting is catalyzed by the presence of alkali. Spectrographic study of the benzenesulfonamide in an alkaline medium at ratio of molar concentrations 2:1 has shown that in this case a doubly charged anion of benzenesulfonamide $(C_6H_5SO_2N)^{=}$ is formed [4].

There is evidently the possibility of simultaneous formation of a singly charged anion $(C_6H_5SO_2NH)^{-}$ which may predominate at different ratios of the alkaline catalyst. Thus, we can assume that salts of arylsulfonamides can react with aldehydes with formation of α-hydroxy derivatives according to the scheme



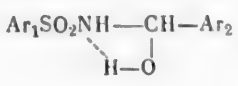
We have studied this reaction for different arylsulfonamides (see table) with p-dimethylamino- and p-diethylaminobenzaldehyde, o-ethoxybenzaldehyde, and m-nitrobenzaldehyde.

The reaction occurs according to the suggested scheme for all the aldehydes studied with mesitylenesulfonamide. For the other arylsulfonamides we have succeeded in isolating the products of the reaction only in the case of dimethylaminobenzaldehyde. The reaction was carried out in anhydrous methyl alcohol in the cold, and with prolonged standing. N-α-hydroxy derivatives precipitated as yellow, well formed crystals. The most active participant in the reaction was mesitylenesulfonamide; in this case reaction occurred in 10-30 minutes, while for the other sulfonamides it took from ten hours to two to three days. Of the arylsulfonamides with nucleophilic substituents, we carried out the reaction with mesitylene, p-toluene, p-chloro, and p-isopropylbenzenesulfonamide. Isopropylbenzenesulfonamide was the least active. Of the arylsulfonamides with electrophilic substituents, we studied m-nitrobenzenesulfonamide. The reaction with this arylsulfonamide takes two days and yields 42% of product. The compounds which we obtained are shown in the table.

$Ar_1SO_2NH - CH(OH)Ar_2$

	Ar_1	Ar_2	Yield, %	M.p.	M found	M calc.	% N found	% N calc.
(I)	C_6H_5	$C_6H_4N(CH_3)_2$	49	197—200°	295	306	9.25	9.16
(II)	p-ClC_6H_4		49.5	164—165	332	340.8	8.20	8.23
(III)	p-$CH_3C_6H_4$		55.8	167—169	316	320.4	8.70	8.74
(IV)	1,2,3-$(CH_3)_3C_6H_2$		63.5	177—177.5	335	348.5	8.10	8.04
(V)	p-$NO_2C_6H_4$		42.5	170—172	315	305.3	9.25	9.19
(VI)	p-$(CH_3)_2CHC_6H_4$		28.8	151—152	335	348.5	8.12	8.04
(VII)	1,2,3-$(CH_3)_3C_6H_2$	$C_6H_4N(C_2H_5)_2$	46.3	105—105.5	372	376.6	7.00	7.45
(VIII)		$C_6H_4OC_2H_5$	43.4	109—111	340	347.5	8.15	8.08

The resulting N-α-hydroxybenzyl derivatives are yellow crystalline substances, soluble in hot alcohol, hot benzene and ligroin, not soluble in carbon tetrachloride, ether, water, or alkali. It is an interesting fact that compounds of this type, as distinguished from the β-hydroxy derivatives and other arylsulfonamide compounds with free hydrogen atoms on the nitrogen of the sulfonamide group, are not titrated by alkali and do not dissolve in it. It can be assumed that this characteristic is caused by the possibility of formation of a hydrogen bond between the hydrogen atoms of the amide group and the oxygen atoms of the hydroxyl group.



In order to confirm the structure of the N-α-hydroxybenzyl derivatives we prepared the products of acylation and of replacement of the hydroxyl group by chlorine in the case of N-α-hydroxydimethylaminobenzylbenzenesulfonamide. Acylation was carried out by boiling with acetyl chloride for one hour. The titration equivalent of the acyl derivative with alkali equals 1; it is soluble in acetic acid and hot water. Chlorine substitution of the product was carried out by action of thionyl chloride and gave a very hygroscopic substance which deliquesced in air and was soluble in hot benzene.

EXPERIMENTAL

Reaction of p-dimethylaminobenzaldehyde with the sodium salts of arylsulfonamides. A mixture of 0.01 mole of Na salt of arylsulfonamide and 0.012 mole of aldehyde was dissolved in anhydrous methyl alcohol and allowed to stand at room temperature until precipitation was complete (from ten hours to two to three days). The solution was treated with 2-3 drops of hydrochloric acid to an acid reaction to Congo, the precipitate was filtered, washed with 5% alkali and water and recrystallized.

Reaction of N-α-hydroxy-p-dimethylaminobenzylbenzenesulfonamide with thionyl chloride. A mixture of 0.002 mole (I) with 0.004 mole of thionyl chloride was heated for two hours in a solution of anhydrous benzene. At the end of the reaction the crystalline precipitate which had formed was filtered and washed with benzene. We obtained 0.7 g of a hygroscopic substance. For analysis we took the wet product.

Found %: Cl 12.80. $C_{15}H_{17}O_2N_2SCl$. Calculated %: Cl 11.00.

Acetylation of N-α-hydroxy-p-dimethylaminobenzylbenzenesulfonamide. A mixture of 0.002 mole (I) with 0.003 mole of acetyl chloride was heated for one hour on a water bath. The precipitate was washed several times with benzene and recrystallized from water. We obtained a product with m. p. 72-73°; the titration equivalent was 1.

SUMMARY

We have obtained and studied N-α-hydroxydimethylbenzylbenzenesulfonamide, N-α-hydroxydimethylbenzyl-p-chlorobenzenesulfonamide, N-α-hydroxydimethylbenzyl-p-toluenesulfonamide, N-α-hydroxydimethylbenzylmesitylenesulfonamide, N-α-hydroxydimethylbenzylisopropylbenzenesulfonamide, N-α-hydroxydimethylbenzyl-m-nitrobenzenesulfonamide, N-α-hydroxydiethylbenzylmesitylenesulfonamide, N-α-hydroxyethoxybenzylmesitylenesulfonamide, and some of their derivatives.

LITERATURE CITED

1. A. E. Kretov and E. A. Abrazhanova, Zhur. Obshch. Khim. 28, 2779 (1958).*
2. D. Peacock and J. Dutt, J. Chem. Soc. (1934), p. 1303.
3. D. Johnson, J. Am. Chem. Soc. 77, 2336 (1955).
4. F. F. Cheshko, Zhur. Obshch. Khim., Sbornik 1, 596 (1953).

* Original Russian pagination. See C. B. translation.

CONDENSATIONS OF 5-HALOFURFUROLS WITH METHYL KETONES

II. CONDENSATIONS WITH ACETOPHENONE AND ITS DERIVATIVES

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Recently there has been great interest in α,β-unsaturated ketones of type (I) not only in connection with their physiological activity [1], but also because of the possibility of their use as intermediates in organic synthesis [2].

$RCH{=}CHCOC_6H_4Y$ (I), where R is aryl, α-thienyl, α-furyl, and Y is H, Cl, Br, OCH_3, OH, NO_2, NH_2, etc.

The condensation of furfurol with acetophenone [3], depending on ratio of reagents and reaction conditions, gives furfurylideneacetophenone (I, X = Y = H), furfurylidenediacetophenone (II), and two isomeric difurfurylidenetriacetophenones (III).

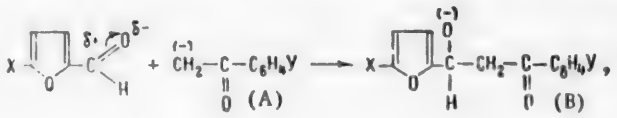
The condensation of furfurol with acetophenone and its substitution products has attracted the further attention of a number of investigators [4]. In studying the rate of reaction between furfurol and acetophenone it was shown that it is directly proportional to the furfurol concentration [5]. The possibility was established of reciprocal replacement of ketones in the condensation products with furfurol, and a method was worked out for the quantitative determination of acetone in the presence of acetophenone, and also of acetophenone in the presence of acetone [6].

The condensation of 5-halofurfurols with acetophenone and its substituted products has not been studied. In view of the rather characteristic behavior of 5-halofurfurols which we showed previously [7], it was of interest to determine the effect of the halogen on the course of the condensation reaction of 5-halofurfurols with acetophenone and its derivatives, the ratio of condensation products to sulfuric acid, and also the effect of the nature of the substituents in the furan and benzene rings on the physiological activity of the preparations.

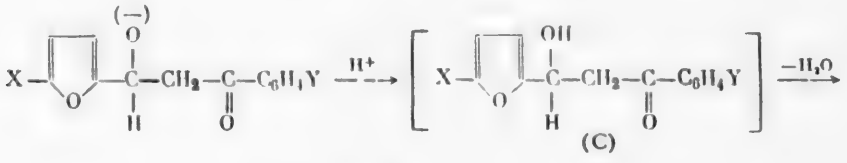
We carried out the condensation of 5-halofurfurols (X = Cl, Br, I) with acetophenone (Y = H), p-chloro- and m-nitroacetophenones (Y = Cl, NO_2) in the presence of both alkaline reagents (caustic alkalis, carbonates, bicarbonates, calcium hydroxide)and of acids (gaseous HCl). However, it was shown that as in the case of acetone [7], acetophenone reacts with 5-halofurfurols only in an alkaline medium. Depending on the ratio of the reagents and the temperature of the reaction (Table 1), we obtained condensation products of type (I), 5-halofurfurylideneacetophenone and type (II), 5-halofurfurylidenediacetophenone.

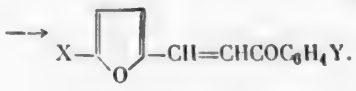
In all cases, independent of the ratio of reacting components (from 1 : 1 to 1 : 10), there were first formed compounds of type (I), and then, according to the scheme given below, compounds of type (II). This was shown by obtaining compounds of type (II) from compounds of type (I) and acetophenone in the presence of alkali solution.

In all probability the reaction goes through the formation of aldols, for the alkaline catalyst removes a proton from the acetophenone molecule with formation of anion (A) which combines with the carbonyl carbon of the halofurfurol.



The resulting anion (B) adds a proton, changing to a molecule of aldol (C).

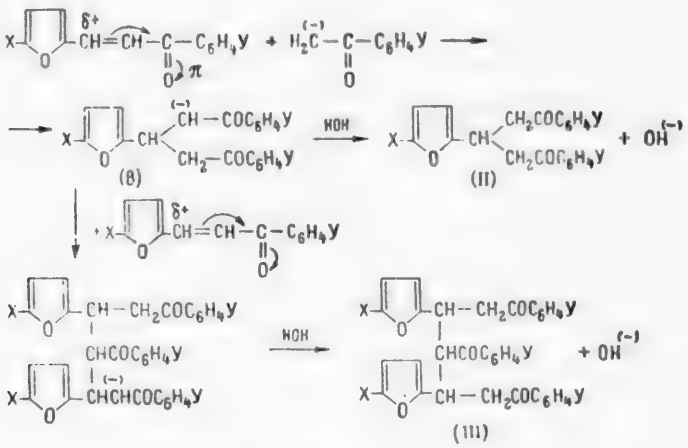




(I)

However, an attempt to separate the aldol has not yet been successful.

The formation of 5-halofurfurylidenediacetophenone (II) shows the rather high activity of the double bond in the α, β-unsaturated ketones with respect to nucleophilic reagent anions as a result of combination of carbon–carbon and carbon–oxygen bonds.



On long standing of alcohol solutions of a mixture of equimolecular amounts of 5-halofurfurylideneacetophenone (I) with 5-halofurfurylidenediacetophenone (II) in the presence of a water solution of alkali, we succeeded in obtaining a high boiling product, in all probability di(5-halofurfurylidene)triacetophenone (III) about which we will report later.

5-Halofurfurylideneacetophenones(I) easily form 2,4-dinitrophenylhydrazones [8]; they dissolve in strong sulfuric acid with formation of a colored solution. However, the influence of substituents (chlorine, bromine, iodine) in the furan ring in position 5 does not have as strong an effect on the change in color of the furfurylideneacetophenone in sulfuric acid as in the case of bis(5-halofurfurylidene) acetone [7], although for it there also exists a minimum concentration of sulfuric acid (Table 1) at which the color begins to occur.

TABLE 1

5-Halofurfurylideneacetophenones $X-(C_4H_2O)-CH=CHCOC_6H_4Y$

Expt. No.	X	Y	Amount of alcohol (ml)	Yield, %	M.p.	M (according to Beckmann) found	M (according to Beckmann) calc.	Percent halogen** found	Percent halogen** calc.	Nature of color with 80% H_2SO_4	Min. conc. H_2SO_4, %	2,4-dinitrophenylhydrazone (from benzene) m.p.	%: N found	%: N calc.	color
1	Cl [10]	H	25	94	107.5—108°	249.5 **	232.7	15.37	15.27	Orange	55.97	204°	13.32	13.57	Bright red
2	Cl	p-Cl *	25	89	134 —135	279.0 **	267.0	29.07	29.17	Straw colored	62.00	172	—	—	"
3	Cl	m-NO_2	60	85	140 —141	269.4	277.5	13.07	13.27	Yellow	60.65	203	—		Red
4	Br [12]	H	40	98	104 —105	269.7	277.2	28.53	28.85	Bright orange	55.97	188—189	12.19	12.25	Bright red
5	Br	p-Cl	40	90	139.5—140	313.4	311.0	39.86	40.13	Yellow	62.00	168	—	—	Orange red
6	Br	m-NO_2	80	87	136 —137	324.5	322.0	24.67	24.84	Yellow with brown tint	60.65	204	—	—	Red
7	I [9]	H	60	96	135 —136	315.5	324.1	39.53	39.19	Greenish-yellow	55.97	194	11.02	11.11	Bordeaux
8	I	p-Cl	60	89	136 —137.5	352.2	358.5	48.07	48.54	Rose-yellow	62.00	192	—	—	"
9	I	m-NO_2	90	84	119 —120	361.9	369.0	34.20	34.42	Yellow with crimson tint	60.65	200	—	—	Orange-red
10	H [13]	m-NO_2	90	90	100 —101	—	—	—	—	Yellow		187—188	—	—	Red
11	H	H	20	80	35 ****	—	—	—	—	Yellow-orange					

* In the synthesis of p-chloroacetophenone instead of carbon disulfide [11] the solvent was excess chlorobenzene. Yield 52%.

** According to Rast.

*** Determined according to [9]; in Experiments 2, 5, 8, we found the total halogen content by the Carius method.

**** Furfurylideneacetophenone was obtained according to [3]; after distillation in a vacuum, m. p. 35° (from ligroin) instead of the literature value of 29° [4b].

5-Halofurfurylideneacetophenones like other 5-substituted furans [9] quantitatively evolve the halogen when heated with HNO_3 (d 1.4). When heated with KI in glacial acetic acid in sunlight, the bromine of 5-bromofurfurylideneacetophenone is easily exchanged with iodine with formation of 5-iodofurfurylideneacetophenone; in the bromination of 5-bromofurfurylideneacetophenone we obtained 3-(5-bromofuryl)-1-phenyl-2,3-dibromopropan-1-one $Br-(C_4H_2O)-CHBr-CHBr-COC_6H_5$ (V), which does not give a colored solution with sulfuric acid.

EXPERIMENTAL

1) 5-Halofurfurylideneacetophenone (I). We dissolved 0.01 mole of the corresponding 5-halofurfurol and acetophenone in a minimum amount of 80% ethanol and with mechanical stirring at 20° we added dropwise 20% aqueous NaOH calculated at 2 ml per 0.01 mole of halofurfurol. After several seconds a precipitate of fine crystals appeared; the mixture was stirred for 30 minutes more, the precipitate was separated,* washed with 10% hydrochloric acid and then with water to a neutral reaction. The use of methanol showed no effect on the yield; sunlight hastened the reaction.

The 5-halofurfurylideneacetophenones did not dissolve in water, were poorly soluble in cold ethyl and methyl alcohols (but easily soluble with heating) and also in ligroin and formic acid; easily soluble in ether, benzene, dichloroethane, carbon tetrachloride, acetone, acetophenone, and glacial acetic acid. After recrystallization from alcohol, yellow crystals (see Table 1) in the form of prisms, not optically homogeneous, showing pleochromism.

2) 3-(5-Bromofuryl)-1-phenyl-2,3-dibromopropan-1-one. To a solution of 2.77 g of 5-bromofurfurylideneacetophenone in 30 ml of CCl_4 with energetic stirring and cooling (7-10°) we added dropwise a solution of 1.6 g of bromine in 20 ml of carbon tetrachloride and poured the mixture into a beaker (for volatilization of the solvent). We obtained 3.5 g (80% from ether without heating) of white plates, m. p. 125-126° (decomposition).

Found %: Br 53.92, 54.04. M 426. $C_{13}H_9O_2Br_3$. Calculated %: Br 54.23. M 437.

3) 5-Halofurfurylideneacetophenone (II). a) A mixture of 0.01 mole of 5-halofurfurol, 0.02 mole of acetophenone, 2 ml of a 40% solution of NaOH and the corresponding amount of ethanol (see Table 2) was heated for 15 minutes on a boiling water bath; with cooling, crystals separated and were filtered and washed with cold aqueous alcohol. White needles from ethanol (Table 2).

TABLE 2

5-Halofurfurylidenediacetophenones $X-(C_4H_2O)-CH(CH_2COC_6H_5)_2$

Expt. No.	X	Amt. of ethanol, ml	Yield, %	M.p.	M found	M calc.	Percent halogen found	Percent halogen calc.
1	Cl	15	75	105-106° (from alcohol)	342.1	352.5	9.88	10.07
2	Br	20	76	100-101° (from ligroin)	400.0	397.3	20.17, 19.86	20.13
3	I	30	70	139-140° (from ligroin)	430.3	444.0	28.23	28.60

b) A mixture of 0.01 mole of 5-halofurfurylideneacetophenone, 0.01 mole of acetophenone, 2 ml of 40% NaOH, and the corresponding amount of ethanol (see Table 2) was heated on a water bath for ten minutes and allowed to stand for six days at room temperature. The precipitate which separated was filtered,

* The filtrate could be used successfully for repeated condensations. Under these conditions the yield decreased by only 1-2%, the cost of solvent and alkali was reduced.

washed repeatedly with water and cold alcohol, and crystallized from ligroin. The 5-halofurfurylidenediacetophenones were white crystalline substances which distilled in a vacuum, easily soluble in most organic solvents (ether, benzene, acetone, acetophenone, glacial acetic acid, carbon tetrachloride, dichloroethane), not soluble in water, poorly soluble in cold ethyl and methyl alcohols but easily so with heating, and also in ligroin and formic acid.

SUMMARY

1. We have shown that, depending on conditions and ratio of reagents, the condensation of 5-halofurfurol with acetophenone can occur with formation of 5-halofurfurylideneacetophenone (yield quantitative) or 5-halofurfurylidenediacetophenone (yield from 70 to 76%).

2. We have obtained nine α,β-unsaturated ketones and three 5-halofurfurylidenediacetophenones which are not described in the literature.

3. We have established that as distinct from bis(5-halofurfurylidene)acetone, the nature of the halogen (Cl, Br, I) in the 5 position of the furan ring does not show much effect on the color of the solution of 5-furfurylideneacetophenone in sulfuric acid.

4. We have shown the possibility of replacement of bromine by iodine in 5-bromofurfurylideneacetophenone.

LITERATURE CITED

1. H. Gilman, L. C. Heckert, A. P. Hewlett, and J. B. Dickey, Zbl. (1933), Vol. II, p. 3126; N. P. Buu-Hoi, N. D. Xuong, and M. Sy, Bull. Soc. Chim. (1956), p. 1646; N. P. Buu-Hoi and M. Sy, Bull. Soc. Chim. (1958), p. 219; Hanson, Referat. Zhur. Khim. (1958), 77630; Sell, Referat. Zhur. Khim. (1959), 8241, and others.
2. R. E. Lyle and L. P. Paradis, J. Am. Chem. Soc. 77, 6667 (1955); A. A. Ponomarev and Z. V. Til', Uch. Zap. SarGU, Vyp. Khim. (1956), No. 43, 53; W. Ried and P. Stahlhofen, Ber. 90, 815 828 (1957); W. Davey and J. R. Gwiet, J. Chem. Soc. (1957), 1008, 1015, 1017, and others.
3. St. v. Kostanecki and L. Podrajansky, Ber. 29, 2248 (1896).
4. a) F. W. Semmler, Ber. 39, 729 (1906); b) A. P. Dunlop and F. N. Peters, The Furans. Am. Chem. Soc. Monograph. Series, No. 119, 36 (New York, 1953).
5. E. K. Nikitin, Zhur. Obshch. Khim. 7, 9 (1937).
6. V. I. Tikgonova, Zhur. Priklad. Khim. 29, 1014 (1949); 23, 1113 (1950);* 24, 202 (1951).*
7. Z. N. Nazarova, Zhur. Obshch. Khim. 27, 2931 (1957).*
8. D. E. Pearson and F. Greer, J. Am. Chem. Soc. 77, 1294 (1955).
9. Z. N. Nazarova, Zhur. Obshch. Khim. 25, 539 (1955).*
10. F. T. Pozharskii, Uch. Zap. Rost. GU, Tr. Khimfaka, X, vyp. 60 (1959).
11. H. Rupe, et al., Ber. 34, 3522 (1901).
12. Z. N. Nazarova, Doklady Akad. Nauk UzSSR (1953), p. 40; Zhur. Obshch. Khim. 24, 575 (1954).*
13. D. L. Furner, J. Am. Chem. Soc. 71, 612 (1949).

* Original Russian pagination. See C. B. translation.

REACTIONS OF TROPYLIUM SALTS WITH SUBSTANCES WHICH CONTAIN MOBILE HYDROGEN ATOMS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1187-1190, April, 1960
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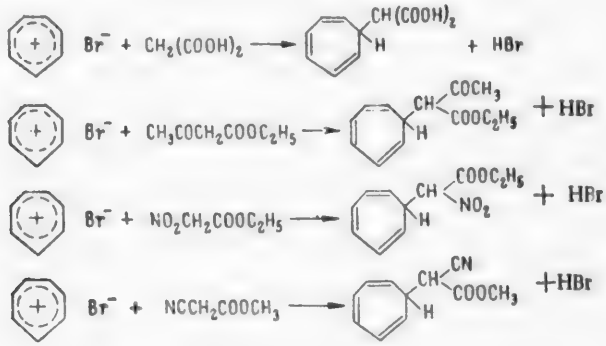
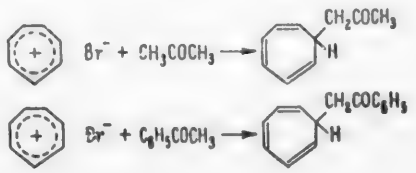
We have recently shown that tropylium salts can easily react with various substances which contain mobile hydrogen in a C–H bond [1]. This reaction, which we have called the tropylation reaction, was studied in greater detail in the case of the reaction of tropylium salts with aliphatic aldehydes [2]. It was shown that the reaction occurs quickly even at room temperature with the formation of cycloheptatrienyl derivatives of aldehydes, and substitution takes place in the α-position to the carbonyl group.

In the present work we have studied the reaction of tropylium bromide with derivatives of carboxylic acids and ketones. We have shown that aliphatic monocarboxylic acids (acetic, propionic, butyric) and their esters (methyl acetate, ethyl acetate, ethyl propionate) even with long heating do not react with tropylium salts. The matter is different with substances in which the mobility of the α-hydrogen atom is increased by the introduction of an activating substituent. Thus, malonic acid, acetoacetic ester, cyanoacetic ester, and nitroacetic ester react rapidly with tropylium salts even at room temperature. In all cases, we found the corresponding products of replacement of one atom of hydrogen by the cycloheptatrienyl residue.


Br⁻ + CH₂(COOH)₂ → CH(COOH)₂ H + HBr
Br⁻ + CH₃COCH₂COOC₂H₅ → CH COCH₃ COOC₂H₅ H + HBr
Br⁻ + NO₂CH₂COOC₂H₅ → CH COOC₂H₅ NO₂ H + HBr
Br⁻ + NCCH₂COOCH₃ → CH CN COOCH₃ H + HBr

Ketones which contain one carbonyl group without activating substituents (acetone, acetophenone) take part in the tropylation reaction under considerably more severe conditions. With prolonged heating of the ketones with tropylium bromide there is replacement of the α-hydrogen atom with formation of monosubstituted products.



The introduction of a second carbonyl group strongly activates the molecule. Thus, for example acetylacetone reacts rapidly with tropylium salts even in the cold.

It is known that by treatment with soda aqueous solutions of tropylium bromide form dicycloheptatrienyl ether [3]. Unlike ordinary ethers, this compound contains a very labile C–O bond and easily splits under the action of mineral acids with the formation of tropylium salts.

$$(C_7H_7)_2O + 2HBr \rightarrow 2C_7H_7^+Br^- + H_2O$$

It has been shown that ditropyl ether can react when heated with acetoacetic ester to form the same product as that from the reaction of tropylium bromide with acetoacetic ester.

EXPERIMENTAL

Cycloheptatrienylacetoacetic ester. To a solution of 1.61 g of tropylium bromide in 25 ml of water was added 1.5 g of acetoacetic ester, and alcohol to the formation of a homogeneous solution. After 30 minutes at room temperature, the reaction had ended (absence of a precipitate with H_2PtCl_6). The solution was diluted with water and extracted with ether. The ether extract, washed with water, was dried over $MgSO_4$. After distillation of the solvent and excess acetoacetic ester we collected 1.24 g (59%) of a substance with b. p. 121.5-124.5° (3 mm), $n^{20}D$ 1.5002. After repeated distillations, the substance had the following constants:

B. p. 121.5° (3 mm), $n^{20}D$ 1.5048, d^{20}_4 1.0601, MR 61.60; calc. 60.30 (for the keto form), 61.34 (for the enol form).

Found %: C 70.81, 70.85; H 7.49, 7.54. $C_{13}H_{16}O_3$. Calculated %: C 70.88; H 7.32.

Cycloheptatrienylacetoacetic ester was also formed in good yield by heating ditropyl ether with acetoacetic ester in benzene.

B. p. 130° (4 mm), $n^{20}D$ 1.5058.

Found %: C 70.95, 70.96; H 7.34, 7.30. $C_{13}H_{16}O_3$. Calculated %: C 70.88; H 7.32.

Ethyl ester of cyclopentatrienylnitroacetic acid. To 3.25 g of tropylium bromide in 25 ml of alcohol was added 3 g of ethyl nitroacetate. After 30 minutes the solution was diluted with water and extracted with ether. The ether extract, washed with water, was dried over $MgSO_4$. After distillation of the solvent and unreacted nitroacetic ester in a vacuum we collected 2.58 g (59.6%) of a substance with b. p. 138-139° (4 mm), $n^{20}D$ 1.5057. After repeated distillations, the substance had the following constants:

B. p. 129° (2 mm), $n^{20}D$ 1.5101, d^{20}_4 1.1522, MR 57.95; calc. 56.66.

Found %: C 59.26, 59.36; H 5.94, 5.98; N 6.24, 6.18. $C_{11}H_{13}O_4N$. Calculated %: C 59.02; H 5.87; N 6.27.

Methyl ester of cycloheptatrienylcyanoacetic acid. To 3.25 g of tropylium bromide in 25 ml of methyl alcohol was added 4 g of methyl cyanoacetate. After two hours the reaction had ended. The methanol solution was diluted with water and the reaction product was extracted with ether.

The ether extract, washed with water, was dried with $MgSO_4$. The solvent and excess cyanoacetic ester were distilled off in a vacuum. We collected 2.01 g (55.9%) of a substance with b. p. 128-132° (3 mm), $n^{20}D$ 1.5164. After repeated distillations we obtained a substance with b. p. 149° (5 mm), $n^{20}D$ 1.5185.

Found %: C 69.51, 69.75; H 5.97, 6.04. $C_{11}H_{11}O_2N$. Calculated %: C 69.82; H 5.85.

Cycloheptatrienylmalonic acid. One g of malonic acid and 1.61 g of tropylium bromide were dissolved in 10 ml of water. After 30 minutes the reaction had ended. The solution was extracted with ether. The ether extract, washed with water, was extracted several times with 5% NaOH solution. The alkaline extract remained for a day with activated charcoal. The alkaline solution was acidified with hydrochloric acid (1 : 1) to an acid reaction to Congo, and was then extracted with ether. The washed and dried ether solution was evaporated in a vacuum. After dilution with ligroin 1.09 g (59%) of cycloheptatrienylmalonic acid precipitated in the form of colorless crystals. The acid was recrystallized from nitromethane. It decomposed violently at 136-137°.

Found %: C 61.64, 61.62; H 5.17, 5.15. M 189.4 (titration). $C_{10}H_{10}O_4$. Calculated %: C 61.84; H 5.19. M 194.2.

Cycloheptatrienylacetone. We boiled 3.25 g of tropylium bromide for two hours in aqueous acetone (30 ml of acetone and 10 ml of water). The reaction solution was diluted with water and extracted with ether. The ether extract, washed with water, was dried with $MgSO_4$. After distillation of the solvent we collected 1.35 g (47.2%) of cycloheptatrienylacetone with b. p. 75.5-76° (2 mm), $n^{20}D$ 1.5236; after repeated distillations the substance had the following constants:

B. p. 70° (2 mm), $n^{20}D$ 1.5243, d^{20}_4 0.9882, MR 45.91; calc. 44.79.

Found %: C 80.87, 80.85; H 8.24, 8.10. $C_{10}H_{12}O$. Calculated %: C 81.04; H 8.16.

The 2,4-dinitrophenylhydrazone had m. p. 161-164° (from alcohol).

Found %: C 58.02, 58.07; H 4.72, 4.87. $C_{16}H_{16}O_4N_4$. Calculated %: C 58.53; H 4.91.

Cycloheptatrienylacetophenone. We boiled 5.21 g of tropylium bromide and 10 g of acetophenone on a water bath for one hour. Considerable tarring occurred. The solution was extracted with ether, washed with water, and dried with $MgSO_4$. After distillation of the solvent in a vacuum, we collected 1.28 g (19.7%) of substance with b. p. 151.5-152° (5 mm).

The 2,4-dinitrophenylhydrazone had m. p. 183.5° (from acetone).

Found %: C 64.91; H 4.67; N 14.61. $C_{21}H_{18}O_4N_4$. Calculated %: C 64.61; H 4.64; N 14.35.

SUMMARY

1. We have shown that tropylium bromide reacts with compounds which contain a mobile hydrogen atom: malonic acid, acetoacetic ester, acetylacetone, nitroacetic ester, methyl cyanoacetate, acetone, and acetophenone.

2. This reaction of tropylation can serve as a general method of synthesis for various cycloheptatrienyl derivatives.

We have obtained cycloheptatrienylmalonic acid, cycloheptatrienylacetoacetic ester, ethyl ester of cycloheptatrienylnitroacetic acid, methyl ester of cycloheptatrienylcyanoacetic acid, cycloheptatrienylacetone, and cycloheptatrienylacetophenone.

LITERATURE CITED

1. M. E. Vol'pin, I. S. Akhrem, and D. N. Kursanov, Izvest. Akad. Nauk SSSR, Otdel Khim. Nauk (1957), p. 1501.*
2. M. E. Vol'pin, I. S. Akhrem, and D. N. Kursanov, Zhur. Obshch. Khim. 29, 2855 (1959).*
3. W. E. Doering and L. H. Knox, J. Am. Chem. Soc. 76, 3203 (1954).

* Original Russian pagination. See C. B. translation.

THE REACTION BETWEEN 1-PHENYL-3-METHYL-3,4-OXIDO-1-BUTYNE AND DIETHYLAMINE

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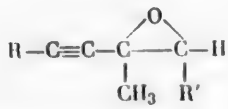
It follows from the work of F. Ya. Perveev and co-workers [1] on the reaction of α-oxides of the acetylene series of the type



with ammonia or amines that there is formed the corresponding amino alcohol or there is direct production of a pyrrole. If a secondary amine is introduced into the reaction, an amino alcohol is formed in which both hydrogens of the amino group are substituted. These amino alcohols are cyclized into N-substituted pyrrole derivatives with migration of one of the radicals on the nitrogen into position 3 of the pyrrole ring [2].

We have studied the reaction of 1-phenyl-3-methyl-3,4-oxido-1-butyne with diethylamine. The oxide was synthesized by the method given in [3]. The reaction was carried out in a sealed glass tube at 100°. It was shown that under these conditions there is both formation of the amino alcohol, and further cyclization of the latter to the pyrrole derivative. After addition to the reaction mixture of p-diazosulfonic acids we were able to isolate a pyrrole azo dye.

During the conversion of the amino alcohol to the pyrrole derivative, it was possible to follow the course of the reaction by determination of active hydrogen at regular intervals of time. After heating for half an hour, the amount of active hydrogen determined by the Terent'ev method, was 0.89, and after three and eight hour heatings, it corresponded to 0.82 and 0.65. If we carried out the reaction at room temperature, noticeable amounts of the pyrrole derivative were not formed. However, in the distillation of the amino alcohol even at a pressure of 0.1-0.01 mm the distillation temperature was sufficiently high to produce formation of traces of pyrrole derivative. This can be shown by depositing the distillate on pine shavings soaked in hydrochloric acid which produces an intense lilac-red color.

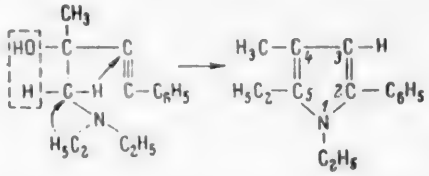
Cyclization of the amino alcohol was carried out in a sealed glass tube at 100°, and also by heating in quinoline at atmospheric pressure in a Wurtz flask at 140-160°. The resulting pyrrole derivative was isolated either by direct fractional distillation or by acidification of the reaction mixture with dilute sulfuric acid and extraction of the pyrrole derivative with n-hexane.

For more detailed characterization of the pyrrole derivative, we synthesized its azo derivative with p-anisidine-diazochloride [4] and p-diazobenzenesulfonic acid [5]. When the first of these diazo compounds acted on the pyrrole derivative, it formed a dark red, flaky precipitate of azo dye, which was converted into the corresponding picrate, reddish, dark lilac scaley crystals.

In the reaction of the pyrrole derivative with p-diazobenzenesulfonic acid in aqueous hydrochloric acid solution there is formed a coral red, crystalline precipitate. When alkali is added, it dissolves and forms a yellow solution, from which acidification again precipitates the red crystals. Reprecipitation from the alkaline solution by addition to it of hydrochloric acid was used to purify the azo dye. We thus obtained the precipitate as red-orange crystals shot with gold. This azo dye was very stable to standing in air and light. After two-year standing in light, often in direct sunlight, no change occurred in the dye.

Neither of these azo dyes gave a characteristic color reaction for α-pyrrole dyes in reaction with diazotized p-nitroaniline [7].

Considering the results of the analyses given below and the reactions and properties of the azo dyes, there is every reason to assume that in the cyclization of the amino alcohol 4-N-diethylamino-1-phenyl-3-methyl-1-butyn-3-ol there is produced N-ethyl-2-phenyl-4-methyl-5-ethylpyrrole, and of the two ethyl groups joined to the nitrogen of the amino alcohol, one migrates in the cyclization not to the 3 position, but to the 5 position. This means that the ethyl group is not joined to the carbon atom which has a free valence when the triple bond is ruptured, as occurs with the acetylene amino alcohols which have a substituent on one carbon of the triple bond [2]. Here the ethyl group dislodges a hydrogen on the carbon bound to the nitrogen and only this hydrogen atom is joined to the carbon which acquires a free valence as a result of rupture of the triple bond. Thus, in this case, cyclization evidently occurs according to the scheme.



It is possible that such an "anomalous" course of the cyclization is connected with the presence of the phenyl group on the triple bond in the original amino alcohol.

EXPERIMENTAL

Synthesis of 4-N-diethylamino-1-phenyl-3-methyl-1-butyn-3-ol. A mixture of 5.0 g of oxide, 5.0 g of diethylamine, and 1 g of water was heated for half an hour in a sealed glass tube at 100°. The reaction mixture separated into two layers. The unreacted diethylamine was removed in a vacuum at 60°. Then the mixture was shaken with a suspension of p-diazobenzenesulfonic acid in 100 ml of water. The orange-red precipitate of pyrrole dye was filtered off. The filtrate was made alkaline and the amino alcohol was extracted with ether. The ether solution was dried with anhydrous Na_2SO_4, the ether was removed on the water bath, and the residue was distilled in a vacuum of about 0.01 mm. We obtained 5.8 g (84%) of a light yellow, oily liquid.

B. p. 120-126° (4 mm), d^{20}_4 0.9685, $n^{20}D$ 1.5292, MR_D 73.02; calc. 71.27.

Found %: N 6.19, 6.25. H_{act} 0.93, 0.92. $C_{15}H_{21}ON$. Calculated %: N 6.05; H_{act} 1.

Picrate of the amino alcohol. Light yellow, needle shaped crystals. After two recrystallizations from alcohol and drying at 90°, m. p. 136.5°.

Found %: N 12.46, 12.34. $C_{21}H_{28}O_8N_4$. Calculated %: N 12.17.

Synthesis of N-ethyl-2-phenyl-4-methyl-5-ethylpyrrole. A mixture of 5.2 g of amino alcohol and 1.2 g of quinoline was heated in a small Wurtz flask for a half hour at 140-160°. Then the quinoline and water were distilled off in a vacuum and the reaction product was fractionated in a vacuum. We obtained 3.2 g (61%) of a light yellow, viscous liquid with an odor resembling that of acetophenone.

When the amino alcohol was cyclized by heating in a sealed glass tube the pyrrole derivative was separated by acidification of the reaction mixture with dilute H_2SO_4 and extraction of the pyrrole derivative with hexane after strong shaking with the added acid. The hexane solution was dried with anhydrous Na_2SO_4, the hexane was distilled off, and the residue was fractionated in a vacuum.

B. p. 103-105° (at 2 mm), d^{20}_4 1.0140, $n^{20}D$ 1.5779.

Found %: N 6.82, 6.87. $C_{15}H_{19}N$. Calculated %: N 6.57.

After two distillations, we obtained a product which was a slightly yellow, oily liquid with an odor resembling that of acetophenone. When this substance was placed on pine shavings soaked in hydrochloric acid, it gave an intense lilac-red color. In the reaction with the Ehrlich reagent it gave a very weak lilac color, and only after long standing, and also with heating, it gave a more intense lilac-blue color. The intense red color characteristic for pyrrole derivatives with free α-positions was not found. The pyrrole derivative did not give a picrate. With $HgCl_2$ [6] it formed a flaky light yellow precipitate.

The mercury derivative, the light yellow, flaky precipitate, was dried in a vacuum over P_2O_5 in the dark for several days. M. p. 59-60° (decomposition).

Found %: N 1.94, 1.91; Cl 17.31; Hg 57.10. $C_{30}H_{36}N_2Hg(HgCl_2)_4$. Calculated %: N 1.64; Cl 16.58; Hg 58.61.

Synthesis of the picrate of N-ethyl-2-phenyl-4-methyl-5-ethylpyrrole-3-azo-4-methoxybenzene was carried out by the method of Reichstein [4]; m. p. 125°.

Synthesis of N-ethyl-2-phenyl-4-methyl-5-ethylpyrrole-3-azo-benzene-4-sulfonic acid was carried out by the method described in [5]. We obtained a coral red azo dye which under the action of alkali became yellow and with acid again became red. It was easily purified by reprecipitation from alkali solution. This process was repeated twice. The needle-shaped orange crystals shot with gold were dried in a vacuum over P_2O_5.

Found %: N 10.92, 10.84. $C_{21}H_{23}O_3N_3S$. Calculated %: N 10.56.

We express our thanks to F. Ya. Perveev for suggesting the theme of our work and for information during the investigation.

SUMMARY

1. We have synthesized for the first time 4-N-diethylamino-1-phenyl-3-methyl-1-butyn-3-ol and shown that in the cyclization of 4-N-diethylamino-1-phenyl-3-methyl-1-butyn-3-ol the ethyl group bound to the nitrogen migrates not to the β-position, but dislodges hydrogen in the α-position and this in turn migrates to the β-position of the pyrrole ring which is formed.

LITERATURE CITED

1. F. Ya. Perveev, E. M. Vekshina, and L. N. Surenkova, Zhur. Obshch. Khim. 27, 1526 (1957);* F. Ya. Perveev and E. M. Kuznetsova, Zhur. Obshch. Khim. 28, 2360 (1958).*
2. F. Ya. Perveev, E. M. Vekshina, and L. N. Surenkova, Vestnik LGU, No. 4, 139 (1957).
3. A. A. Ivanova, Zhur. Obshch. Khim. 17, 1116 (1947).
4. T. Reichstein, Helv. Chim. Acta 10, 387 (1927).
5. H. Fischer and E. Bartholomäus, Ber. 45, 1919 (1912).
6. H. Fischer and R. Müler, Z. Physiol. Chem. 148, 164 (1925).
7. Heterocyclic Compounds, I, 240 (IL, 1953); H. Fisher and G. Ort, Chemistry of Pyrrole [Russian translation] (ONTI, 1937).

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SYNTHESIS OF SOME α-OXIDES OF THE ACETYLENIC SERIES

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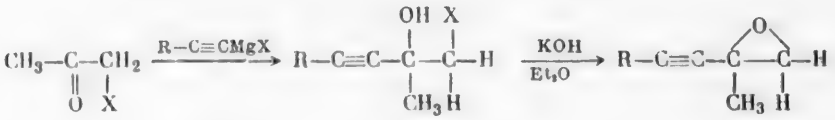
The aim of the present work was the synthesis by the following route [1, 2] of 2-methyl-1,2-epoxy-3-octyne and 2,7-dimethyl-1,2-epoxy-2-octyne. These compounds and the starting halohydrins have not been described in the literature.



The starting acetylenic hydrocarbons – 1-hexyne and 5-methyl-1-hexyne – were prepared from sodium acetylide and the corresponding alkyl bromide in liquid ammonia [3]. For the synthesis of 1-bromo-2-methyl-3-octyn-2-ol we started from bromoacetone and 1-hexyne. 1-Chloro-2,7-dimethyl-3-octyn-2-ol was synthesized from chloroacetone and 5-methyl-1-hexyne. The lower yield of bromohydrin is due to the bigger part played by secondary reactions. Synthesis of 2-methyl-1,2-epoxy-3-octyne and 2,7-dimethyl-1,2-epoxy-3-octyne from the corresponding halohydrins in presence of KOH powder in absolute ether proceeds smoothly.

EXPERIMENTAL

Preparation of 1-bromo-2-methyl-3-octyn-2-ol. To a solution of hexynemagnesium bromide, prepared from 24 g of Mg, 110 g of ethyl bromide and 1-hexyne, was added bromoacetone dropwise with stirring in the course of an hour while the flask was cooled with water. Stirring was continued at room temperature for another few hours and the mass was stood for three days. The resulting complex was decomposed with 30% sulfuric acid, and then the mixture was extracted with three portions of ether (150 ml each). The combined ethereal extracts were dried with sodium sulfate, the ether was driven off, and the residue distilled in vacuo. A colorless, oily liquid came over and acquired a lilac-red color after standing for a short time. It had a clinging sweet odor. On standing, it darkened and turned green. Yield 100 g (46%). The product was distilled twice.

B. p. 109-110° (10 mm), d^{20}_4 1.2497, $n^{20}D$ 1.4911, MR_D 50.76; calc. 50.99.

Found: number of active H atoms: 0.92, 0.92. $C_9H_{15}OBr$. Calculated: number of H atoms 1.0.

Preparation of 1-chloro-2,7-dimethyl-3-octyn-2-ol. Components taken for the synthesis were 48 g of 5-methyl-1-hexyne, 55 g of ethyl bromide, 12 g of Mg and 46 g of chloroacetone. The chloroacetone was added in the course of an hour. Stirring was continued at room temperature. A heavy, dark-green oil settled to the bottom of the flask and was allowed to stand for 4 days. It was then worked up as in the preceding experiment. The product was a colorless liquid with a clinging sweet odor. It became greenish-yellow on standing. The product was distilled twice.

B. p. 105-107° (10 mm), d^{20}_4 0.9856, $n^{20}D$ 1.4672, MR_D 53.04; calc. 52.83.

Found: number of active H atoms: 1.08, 0.90. $C_{16}H_{17}OCl$. Calculated: number of active H atoms: 1.0.

Preparation of 2-methyl-1,2-epoxy-3-octyne. A solution of 100 g of 1-bromo-2-methyl-3-octyn-5-ol in 300 ml of absolute ether was made up in a 750 ml flask, and 170 g of potassium hydroxide powder was added in small portions. After each addition of alkali, the flask was cooled with water and shaken. The reaction was assumed complete when the ethereal solution gave a negative Beilstein test for halogen. The precipitate was filtered and washed a number of times on the filter with ether. The ethereal solution was dried with calcined potassium carbonate, the ether was driven off and the residue fractionated in vacuo. Two distillations gave a colorless liquid with a characteristic sweet odor. Yield of oxide 54 g (86%).

B. p. 67-68° (10 mm), d^{20}_4 0.8907, $n^{20}D$ 1.4492, MR_D 41.60; calc. 41.84.

Found %: C 78.10; H 10.34. $C_9H_{14}O$. Calculated %: C 78.26; H 10.14.

Preparation of 2,7-dimethyl-1,2-epoxy-3-octyne was carried out by the preceding procedure starting from 64 g of the corresponding chloro alcohol, 300 ml of absolute ether and 100 g of potassium hydroxide. Two distillations in vacuo gave a liquid with a characteristic sweet odor. Yield 45 g (70.5%).

B. p. 75-76° (9 mm), d^{20}_4 0.8732, $n^{20}D$ 1.4481, MR_D 46.63; calc. 46.46.

Found %: C 78.70; H 10.67. $C_{10}H_{16}O$. Calculated %: C 78.90; H 10.55.

I express my deep gratitude to F. Ya. Perveev for suggesting the subject of this investigation and for his guidance during the work.

SUMMARY

The following compounds were synthesized for the first time: 1-bromo-2-methyl-3-octyn-2-ol, 1-chloro-2,7-dimethyl-3-octyn-2-ol, 2-methyl-1,2-epoxy-3-octyne, 2-methyl-1,2-epoxy-3-octyne, and 2,7-dimethyl-1,2-epoxy-3-octyne.

LITERATURE CITED

1. F. Ya. Perveev, Zhur. Obshch. Khim. 18, 481 (1948).
2. F. Ya. Perveev, Zhur. Obshch. Khim. 19, 1304 (1949).*
3. T. H. Vaughan, R. R. Vogt, and J. A. Nieuwland, J. Am. Chem. Soc. 56, 2120 (1934).

*Original Russian pagination. See C. B. translation.

HETEROCYCLIC COMPOUNDS

SYNTHESIS OF p-METHOXYPHENOXYACETIC ESTERS OF THE α-FORM OF 1-ALLYL- AND 1-CROTYL-2,5-DIMETHYL-4-PIPERIDOLS

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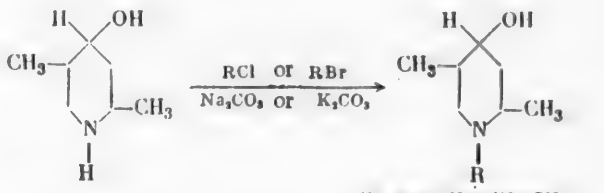
Original article submitted April 3, 1959

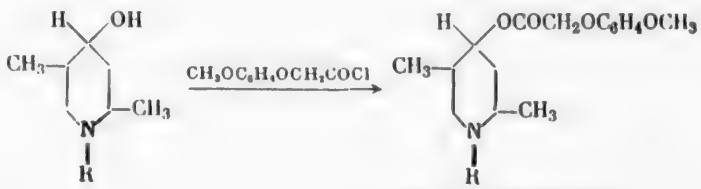
In the preceding communication [1] were described several esters of the α-form of secondary 1-alkenyl-2,5-dimethyl-4-piperidols, among which were detected a series of compounds possessing powerful anesthetizing action. In the present work, we synthesized the p-methoxyphenoxyacetic esters of the α-form of 1-allyl- and 1-crotyl-2,5-dimethyl-4-piperidols (III, IV) with the object of investigating the influence of an acyl residue on the pharmacological properties of these esters.

The starting 1-alkenyl-2,5-dimethyl-4-piperidols (I, II) which have been described previously [1], were prepared in high yields (over 80%) by alkenylation with the corresponding allylic halogen derivatives of the α-form of 2,5-dimethyl-4-piperidol [2, 3] in solution in anhydrous solvents (acetone, 1-butanol) in presence of alkaline agents (sodium carbonate, potassium carbonate).



(I) R = CH_2=CH–CH_2.
(II) R = CH_3CH=CH–CH_3.

Esterification of 1-alkenyl-2,5-dimethyl-4-piperidols (I, II) with p-methoxyphenoxyacetyl chloride gave the corresponding esters (III, IV).



(III) R = CH_2=CH–CH_2.
(IV) R = CH_3CH=CH–CH_3.

EXPERIMENTAL

1-Allyl-2,5-dimethyl-4-piperidol (I). In the course of 30 minutes a solution of 8.4 g of allyl chloride in 10 ml of anhydrous 1-butanol was added dropwise with stirring to a solution of 14.8 g of the α-form of 2,5-dimethyl-4-piperidol (m. p. 96-97°) in 240 ml of anhydrous 1-butanol to which had previously been added 12.7 g of anhydrous sodium carbonate in powder form. The reaction mixture was stirred and heated for 8 hours at 80° and then left overnight. The precipitate was filtered off and washed several times with ether. The 1-butanol and the ether were distilled off, the residue was dissolved in ether, and the ethereal solution washed with 20 ml of water. After the solution had been dried, the ether was driven off and the residue distilled to give 16.05 g (83.2%) of 1-allyl-2,5-dimethyl-4-piperidol in the form of a viscous liquid with b. p. 98° (2 mm), $n^{20}D$ 1.4843. After cooling it crystallized to low-melting (m. p. 29-30°) crystals which could not be recrystallized. The hydrochloride melted at 215-216°.

1-Crotyl-2,5-dimethyl-4-piperidol (II). A solution of 6 g of primary crotyl bromide ($n^{20}D$ 1.4805) [4] in 20 ml of anhydrous acetone was stirred at 50-55° dropwise into a mixture of 5.16 g of the α-form of 2,5-dimethyl-4-piperidol (b. p. 96-97°) in 150 ml of anhydrous acetone and 5.52 g of anhydrous potassium carbonate in powder form. After 4-hour heating at 50-55°, the mass was stood overnight. The precipitate was filtered off and washed with dry acetone. The acetone was driven off from the filtrate; the residual viscous mass crystallized. Two recrystallizations gave 6.2 g (84.7%) of the α-form of 1-crotyl-2,5-dimethyl-4-piperidol with m. p. 91-92° (from gasoline). The hydrochloride melted at 196-197° (from a mixture of alcohol and ether) [1].

p-Methoxyphenoxyacetic ester of the α-form of 1-allyl-2,5-dimethyl-4-piperidol (III). A mixture of 3.4 g of the α-form of 1-allyl-2,5-dimethyl-4-piperidol (m. p. 29-30°) in 5 ml of anhydrous benzene and 6 g of p-methoxyphenoxyacetyl chloride was heated for 10 hours at 110-115°. After 20 ml of benzene had been added, the mass was stood overnight. The precipitate was filtered off, washed with benzene, and twice recrystallized from acetone (once after boiling in presence of active carbon). There was obtained 2.6 g of the hydrochloride of the p-methoxyphenoxyacetic ester of the α-form of 1-allyl-2,5-dimethyl-4-piperidol with m. p. 159-160°.

Found %: N 3.57, 3.81; Cl 9.28, 9.27. $C_{19}H_{28}O_4NCl$. Calculated %: N 3.79; Cl 9.58.

p-Methoxyphenoxyacetic ester of the α-form of 1-crotyl-2,5-dimethyl-4-piperidol (IV). To a solution of 2.75 g of the α-form of 1-crotyl-2,5-dimethyl-4-piperidol (m. p. 91-92°) in 5 ml of anhydrous benzene was added 6 g of p-methoxyphenoxyacetyl chloride (b. p. 132-134° at 2 mm). The reaction mixture was heated for 10 hours at 110-115° and then stood overnight. The precipitate was filtered off and twice recrystallized from acetone to give 1.6 g of the hydrochloride of the p-methoxyphenoxy ester of the α-form of 1-crotyl-2,5-dimethyl-4-piperidol with m. p. 162-163° (from acetone).

Found %: N 3.65, 3.36; Cl 9.33, 9.51. $C_{20}H_{30}O_4NCl$. Calculated %: N 3.65; Cl 9.23.

SUMMARY

1. Alkenylation of 2,5-dimethyl-4-piperidol in anhydrous solvents (acetone, 1-butanol) in presence of alkaline agents (sodium or potassium carbonate) with unsaturated halogen derivatives gave high yields of 1-alkenyl-2,5-dimethyl-4-piperidols – 1-allyl- and 1-crotyl-2,5-dimethyl-4-piperidols – previously described by us.

2. The p-methoxyphenoxyacetic esters of the α-form of 1-allyl- and 1-crotyl-2,5-dimethyl-4-piperidols were synthesized.

LITERATURE CITED

1. I. N. Nazarov, A. Sh. Sharifkanov, and K. F. Danilova, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1958), p. 739.*
2. I. N. Nazarov and V. A. Rudenko, Zhur. Obshch. Khim. 22, 829 (1952).*
3. I. N. Nazarov, D. V. Sokolov, and V. N. Rakcheeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1954), p. 80.*
4. W. G. Young and U. S. Winstein, J. Am. Chem. Soc. 57, 2013 (1935).

* Original Russian pagination. See C. B. translation.

ACETYLENIC AMINO ALCOHOLS

I. PREPARATION OF 1,1-DISUBSTITUTED 4-DIALKYLAMINO-2-BUTYN-1-OLS

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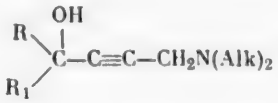
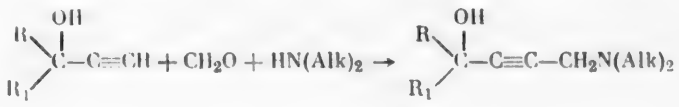
Substituted aminobutynols with the general formula



are of definite interest as substances that can be expected to possess considerable physiological activity. These compounds also permit transition to a series of substances (products of their hydrogenation, hydration, etc.) not easily synthesized by other routes. Some of these derivatives might also possess high physiological activity (cholinolytic in particular). The synthesis of some substituted aminobutynols has been reported in [1, 2].

The most attractive route for their synthesis might appear to be the aminomethylation of tertiary ethynylcarbinols by the Mannich reaction.



Compounds with a primary acetylenic group usually enter into this reaction with facility, but diarylethynylcarbinols give products of aminomethylation at the acetylenic group only in negligible yield [1].

It has also been shown that alkyl-substituted acetylenic alcohols (and glycols), under the conditions of the Mannich reaction, form products of aminomethylation at the hydroxy group – the corresponding dialkylaminomethyl ethers [3]. Amino alcohols were not found among the reaction products.

The cause of this passivity of the acetylenic group in tertiary ethynylcarbinols is considered to be the free hydroxyl [1]. It is true that when alcohols are converted to β-cyanoethyl ethers [4], β-cyanoethoxyethyl ethers [5] or acetic esters [1], the resulting derivatives are capable of undergoing the Mannich reaction. However, the only representatives of the foregoing types of derivatives that can be utilized for the preparation of substituted aminobutynols are the acetates of the carbinols, since there is no convenient method of elimination of the β-cyanoethyl and β-cyanoethoxyethyl groups. But even such a route is not very suitable: the yield of substituted amino alcohol is not very high and the acetyl derivatives themselves (particularly in the case of aryl-substituted carbinols) are obtained with difficulty.

Shvekhgeimer [6] has proposed a convenient method of preparation of substituted aminobutynols. Treatment of ethynylcarbinols with vinyl ethyl ether leads to mixed acetals which also enter into the Mannich reaction; the

acetal group is then split off without difficulty by dilute mineral acid. Yields at all steps are high. A defect of the method is the extremely long period of aminomethylation (boiling of the dioxane solution of the reactants for 80-115 hours).

With the aim of improving the synthesis of substituted dialkylaminobutynols we made a detailed investigation of the possibility of aminomethylation of the tertiary ethynylcarbinols themselves. It was found that in presence of small amounts of copper compounds (which are frequently used as catalysts in the Mannich reaction [7]) they smoothly undergo aminomethylation. Reaction is rapid under mild conditions and products are obtained directly in sufficient purity and good yields. Application of the method to alkyl-substituted ethynylcarbinols does not lead to aminomethylation at the hydroxy group but only to derivatives of aminobutynols (the reaction products do not contain a primary acetylenic group). In all cases, the catalytic action is evidently exerted by monovalent copper (possibly in the form of intermediate acetylides). If salts of divalent copper can be easily reduced by formaldehyde under the reaction conditions (alkaline medium), then their action does not differ in practice from that of monovalent copper. In neutral or weakly acid media (amine salt) divalent copper is not easily reduced and its use then leads to lower yields. The amount of catalyst does not affect the yield if it is not below a certain level; smaller amounts cannot be compensated for by more prolonged heating.

We made use of two procedures for aminomethylation. In one procedure (the more general one) the acetylenic alcohol was treated with an aqueous solution of formaldehyde (formalin) and with a salt of the corresponding amine (hydrobromides often gave higher yields than hydrochlorides) in presence of copper acetylide, which under these conditions gave the best results. If the starting carbinol was poorly soluble in water, then a suitable organic solvent (usually ethanol) was added in the necessary quantity in order to obtain a homogeneous mass. The second procedure consisted in the use of a mixture of the free amine and polyoxymethylene. This gives a faster reaction but is often accompanied by resinification; the procedure is therefore limited in application. A solvent is essential in this variant because otherwise the yield is lowered and the product is contaminated by resins. Dioxane as a solvent gives better results than alcohol. In this procedure Cu_2C_2 and CuCl are nearly equivalent as catalysts; sometimes cuprous chloride leads to a slightly higher yield.

Seven amino alcohols were obtained by this method: 2-methyl-5-diethylamino-3-pentyn-2-ol (I), 3-methyl-6-diethylamino-4-hexyn-3-ol (II), 1,1-diphenyl-4-diethylamino-2-butyn-1-ol (III), 1,1-diphenyl-4-piperidino-2-butyn-1-ol (IV), 1,1-diphenyl-4-dimethylamino-2-butyn-1-ol (V), 1-diethylamino-3-(9'-hydroxy-9'-fluorenyl)-2-propyne (VI), and 1-phenyl-1-cyclohexyl-4-diethylamino-2-butyn-1-ol (VII). Two of these (III, IV) were synthesized by another route in order to obtain confirmation of the structure of the amino alcohols.

According to [8] the treatment of diethylamino-2-bromopropene with two moles of sodium amide in liquid ammonia gives the sodium derivative of diethylpropargylamine $(C_2H_5)_2NCH_2C \equiv CNa$. The free acetylenic amine was isolated by treatment of the sodium compound with water, but it can also be immediately alkylated for the purpose of obtaining disubstituted acetylenes.

We utilized the resulting sodium derivative of diethylaminopropyne for synthesis of aminobutynols by treating its solution in liquid ammonia with an ethereal solution of benzophenone. Amino alcohols were thereby formed in good yield. They were found to be identical with the products obtained by aminomethylation. In some cases, this route may be more convenient for the preparation of substituted aminobutynols than the Mannich reaction.

EXPERIMENTAL

The starting acetylenic carbinols were synthesized by the literature methods – sometimes slightly modified. Their properties agreed with those reported previously. The authors obtained 3-methyl-4-pentyn-3-ol from Kh. V. Bal'yan to whom we convey our thanks.

2-Methyl-5-diethylamino-3-pentyn-2-ol (I). Reaction components were 3 g of 2-methyl-3-butyn-2-ol [8], 4 g of diethylamine hydrochloride, 10 ml of formalin and 0.08 g of copper acetylide (carefully pulverized beforehand) [9]. These were heated on a water bath at 80-90° for 2 hours. After the mass had cooled, it was made alkaline with aqueous potassium carbonate and extracted several times with ether. The extract was dried with potassium carbonate and fractionated to give 4.9 g (81.2%) of the amino alcohol.

B. p. 92° (4 mm), 104° (10 mm), $n^{20}D$ 1.4614. Literature [6]: b. p. 72-73° (2 mm), $n^{20}D$ 1.4634.

3-Methyl-6-diethylamino-4-hexyn-3-ol (II). The preceding procedure was applied to a mixture of 8 g of 3-methyl-4-pentyn-3-ol, 9.5 g of diethylamine hydrochloride, 20 ml of formalin and 0.12 g of copper acetylide. There was obtained 12.03 g (80.6%) of amino alcohol with b. p. 105.5-106° (8 mm), $n^{20}D$ 1.4650.

Literature data [6]: b. p. 79-80° (2 mm), $n^{20}D$ 1.4661.

1,1-Diphenyl-4-diethylamino-2-butyn-1-ol (III). a) Mannich reaction. A mixture of 1 g of diphenylethynylcarbinol [10], 0.2 g of polyoxymethylene, 0.4 g of diethylamine and 0.01 g of cuprous chloride in 5 ml of dioxane was heated on a water bath for 1.5 hours. The cooled solution was poured into dilute hydrochloric acid and thoroughly shaken; the nonbasic compounds were then extracted with ether. The aqueous layer was made alkaline with ammonia solution and extracted with ether. After drying with potassium carbonate, the ether was driven off to leave a residue of 1.21 g (86%) of nearly colorless crystals with m. p. 94.5-96°. Recrystallization from hexane gave 1.17 g of substance with m. p. 96.5-97.5°. Further recrystallizations did not raise the melting point.

b) From diethylamino-2-bromo-2-propene and benzophenone. To a suspension of sodium amide in 100 ml of liquid ammonia (prepared from 2.2 g of sodium) was added 8 g of diethylamino-2-bromo-2-propene [8] in 5-10 minutes. The solution was then stirred for 3 hours. Loss of ammonia by evaporation was made good by addition of fresh portions. Dropwise addition was then made of 7.6 g of benzophenone in 50 ml of absolute ether. The mass was stirred until all the ammonia had gone off, and the residue was heated for 1.5 hours to complete the reaction. After cooling, the mixture was hydrolyzed by careful addition of water. The ether layer was twice extracted with dilute hydrochloric acid, the aqueous layer made alkaline, and the amino alcohol extracted with chloroform. The extract was dried and the solvent distilled off to leave 7.82 g (65% calculated on the diethylaminobromopropene) of brown crystals with m. p. 75-85°. Subsequent crystallizations from hexane (or a little alcohol) gave a pure product that did not give a melting point depression in admixture with the aminoalcohol prepared by the Mannich reaction.

Found %: N 4.90, 4.86. $C_{20}H_{23}ON$. Calculated %: N 4.77.

The hydrochloride was prepared by the usual method; m. p. 174.5-175° (from dioxane).

Found %: Cl 10.65, 10.68. $C_{20}H_{24}ONCl$. Calculated %: Cl 10.75.

1,1-Diphenyl-4-(N-piperidino)-2-butyn-1-ol (IV). a) By Mannich reaction. A mixture of 1 g of diphenylethynylcarbinol, 0.8 g of piperidine hydrobromide, 1.5 ml of formalin, 0.01 g of acetylide and 5 ml of ethanol was heated for 4 hours on a water bath at 80-90°. At the end of the reaction, the mixture was run into water and acidified with a little hydrochloric acid. Further treatment was as in the preparation of alcohol (III). The amino alcohol was extracted with chloroform. Yield 1.28 g (87.5%) of crystals with m. p. 134.5-135.5°. Recrystallization from dibutyl ether gave 1.15 g of pure substances with m. p. 135.5-136.5°. The melting point did not change after further recrystallizations.

b) From N-piperidino-2-bromo-2-propene. The procedure was the same as for the reaction of diethylaminobromopropene with benzophenone. From 2.1 g of sodium, 8.1 g of piperidinobromopropene (synthesized on the same lines as diethylaminobromopropene in 79.5% yield, b. p. 87° at 10 mm) and 7.25 g of benzophenone was obtained 9.26 g (76.5% on the original amine) of substance with m. p. 131-133°. No depression of melting point in admixture with the amino alcohol prepared by the Mannich reaction.

Found %: N 4.75, 4.77. $C_{21}H_{23}ON$. Calculated %: N 4.59.

The hydrochloride had m. p. (after several recrystallizations from isopropyl alcohol) 199-200° (decomp.).

Found %: Cl 10.45, 10.43. $C_{21}H_{24}ONCl$. Calculated %: Cl 10.37.

1,1-Diphenyl-4-dimethylamino-2-butyn-1-ol (V). Prepared similarly to alcohol (IV) from 1 g of diphenylethynylcarbinol, 0.42 g of dimethylamine hydrochloride, 1.5 ml of formalin, 0.05 g of pulverized copper acetylide, and 5 ml of alcohol; reaction period 1.5 hours. Yield 1.04 g (81.8%) of yellowish substance with m. p. 137-139°. Recrystallization from dibutyl ether gave 0.97 g of colorless needles with m.p. 140.5-141.5. The melting point rose to 141-142° after further recrystallizations from the same solvent or gasoline [2].

Found %: N 5.30, 5.35. $C_{18}H_{19}ON$. Calculated %: N 5.30.

The hydrochloride had m. p. 200.5-201° (decomp.) after several recrystallizations from n-butyl alcohol.

Found %: Cl 11.94, 11.81. $C_{18}H_{20}ONCl$. Calculated %: Cl 11.75.

1-Diethylamino-3-(9'-hydroxy-9'-fluorenyl)-2-propyne (VI). A mixture of 1 g of 9-hydroxy-9-ethynylfluorene [11], 0.2 g of polyoxymethylene, 0.4 g of diethylamine, 0.01 g of copper acetylide and 5 ml of dioxane was heated on a water bath for an hour. To the hot solution was then added a further 3-4 ml of dioxane and the solution was filtered hot. The cooled solution deposited 1.12 g of colorless crystals with m. p. 204-205° (79.5%). Further recrystallizations from dioxane gave the perfectly pure substance with m. p. 208.5-209° (slight decomp.).

Found %: N 4.78, 4.90. $C_{20}H_{21}ON$. Calculated %: N 4.81.

The hydrochloride was crystallized several times from isopropyl alcohol. M. p. 213-214°.

Found %: Cl 10.63, 10.73. $C_{20}H_{22}ONCl$. Calculated %: Cl 10.82.

1'-Phenyl-1-cyclohexyl-4-diethylamino-2-butyn-1-ol (VII). From 1 g of phenylcyclohexylethynylcarbinol [12], 0.2 g of polyoxymethylene, 0.4 g of diethylamine, 0.01 g of copper acetylide and 5 ml of dioxane was obtained [under the same conditions as for synthesis of (III)] 1.34 g (95.8%) of product with m. p. 80-84°. Crystallization from hexane gave 1.20 g of substance with m. p. 86.5-87°.

Found %: N 4.80, 4.81. $C_{20}H_{29}ON$. Calculated %: N 4.68.

Hydrochloride: m. p. 168° (from acetone).

Found %: Cl 10.59, 10.63. $C_{20}H_{30}ONCl$. Calculated %: Cl 10.56.

SUMMARY

1. It was shown that tertiary acetylenic carbinols are capable of entering into the Mannich reaction in presence of catalysts (copper compounds) and of giving high yields of substituted aminobutynols.

2. Seven substituted aminobutynols were obtained by this route, including four not described in the literature: 1,1-diphenyl-4-diethylamino-2-butyn-1-ol, 1,1-diphenyl-4-piperidino-2-butyn-1-ol, 1-diethylamino-3-(9'-hydroxy-9'-fluorenyl)-2-propyne, 1-phenyl-1-cyclohexyl-4-diethylamino-2-butyn-1-ol.

3. The same substituted amino alcohols could also be prepared in satisfactory yields from dialkylamino-2-bromo-2-propenes by the action of sodium amide and the corresponding ketones.

4. Hydrochlorides of some of the synthesized aminobutynols were prepared.

LITERATURE CITED

1. H. P. W. Huggill and J. D. Rose, J. Chem. Soc. (1950), p. 335.
2. U. S. Patent 2,584,429; Chem. Abs. (1952), 9605 h.
3. E. S. Lagucheva, Zhur. Obshch. Khim. 27, 1518 (1957).*
4. E. S. Lagucheva and K. D. Petrov, Zhur. Obshch. Khim., Supplem. Vol. II, 1347 (1953).
5. I. N. Nazarov and G. A. Shvekhgeimer, Zhur. Obshch. Khim. 26, 813 (1956).*
6. G. A. Shvekhgeimer, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1957), p. 1265.*
7. Symposium on Acetylene Chemistry [Russian translation] (IL, 1954), p. 281.
8. R. F. Parcell and C. B. Pollard, J. Am. Chem. Soc. 72, 2385 (1950).

* Original Russian pagination. See C. B. translation.

9. L. Vanino, Handbuch der präparativen Chemie (Stuttgart, 1925), 1, 517.
10. D. Papa, F. J. Villani, and H. F. Ginsberg, J. Am. Chem. Soc. 76, 4446 (1954).
11. G. F. Hennion and B. R. Fleck, J. Am. Chem. Soc. 77, 3253 (1955).
12. M. Harfenist and E. Magnien, J. Am. Chem. Soc. 78, 1060 (1956).

INTERACTION OF ACETYLENIC CARBINOLS WITH ACETIC ACID IN PRESENCE OF MERCURIC ACETATE AND THE MECHANISM OF FORMATION OF ACETOXY KETONES

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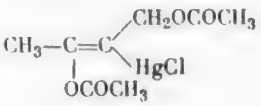
I. N. Nazarov [1] and G. Hennion [2] showed almost simultaneously that tertiary acetylenic alcohols are converted into acetates of acetylcarbinols in glacial acetic acid solution in presence of boron trifluoride and mercuric oxide.

In the present work, we developed a more convenient method of preparation of acetoxy ketones by boiling acetic acid solutions of acetylenic alcohols in presence of mercuric acetate and subsequently fractionating the reaction mixture. In this manner the corresponding acetates of tertiary acetylcarbinols were prepared from dimethyl-, methylethyl-, methylisopropyl-, diisopropyl-, and methylphenylethynylcarbinols, as well as from 1-ethynylcyclohexan-1-ol. Heating of a disubstituted acetylenic alcohol – 2-butyn-1-ol – with glacial acetic acid in presence of mercuric acetate gave methyl-β-acetoxyethyl ketone.

It is interesting to note that 3-phenyl-2-propyn-1-ol and 4,4-dimethyl-2-pentyn-1-ol also give β-keto derivatives under hydration conditions in presence of mercuric acetate and 60% acetic acid, as shown by E. D. Venus-Danilova and S. N. Danilov [3].

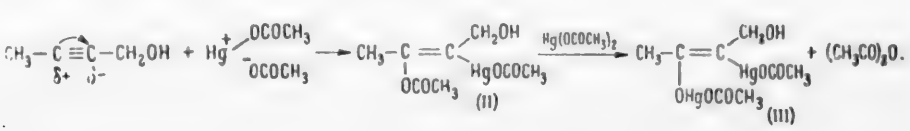
We know that both monosubstituted and disubstituted acetylenes in a neutral or weakly acid medium react with mercuric acetate to form polymercurated compounds which on heating with acetic acid or with dilute mineral acids are converted to ketones [4]. Formation of acetoxy ketones from acetylenic alcohols in presence of mercuric acetate evidently proceeds via analogous organomercury compounds as we proved in the case of the acetate of 2-butyn-1-ol.

Reaction of 2-butyn-1-ol acetate with mercuric acetate gave an addition product (a chloromercuro compound) (I).

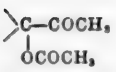


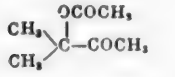
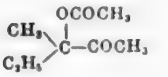
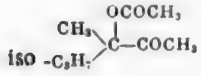
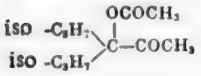
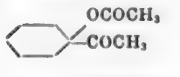
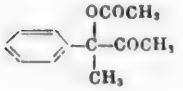
(I)

Due to one-sided polarization of the triple bond, the original product of addition of mercuric acetate to 2-butyn-1-ol corresponds to structure (II). Acetic anhydride appears to be formed when this adduct is converted in an anhydrous medium into the dimercuro compound (III).

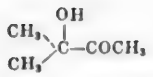
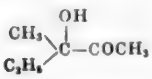
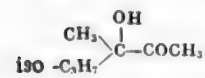
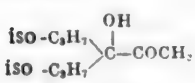
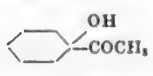
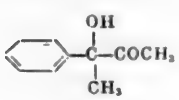


(II) (III)

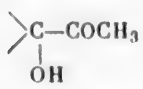
Acetoxy Ketones 

Formula	Yield, %	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
	87	60— 62° (10)	1.4155	—
	75	72— 73 (9.5)	1.4240	0.9988
	72	84— 85 (10)	1.4292	0.9903
	78	94— 96 (10)	1.4400	0.9767
	97	84— 86 (2.5)	1.4596	—
	50	102—105 (2)	1.5055	1.0930

α-Ketoalcohols

	92	140—141 (680)	1.4140	—
	88	40— 42 (10)	1.4200	—
	85	48— 50 (9.5)	1.4250	0.9356
	80	68— 70 (9)	1.4388	—
	90	86— 88 (9)	1.4693	—
	75	89— 91 (2.5)	1.5230	—

MR		Analysis (in %)				2,4-Dinitrophenylhydrazones			Literature references
		found		calc.			% N		
found	calc.	C	H	C	H	melting point	found	calc.	
—	—	—	—	—	—	144—145°	17.43, 16.59	17.29	[1]
40.37	40.80	60.58, 60.52	8.79, 9.09	60.76	8.86	131—132	16.94, 17.08	16.56	—
44.79	45.42	62.25, 62.54	9.23, 9.28	62.79	9.30	117—119	15.97, 16.03	15.90	—
53.97	54.66	65.43, 65.74	9.79, 10.00	66.09	10.00	—	—	—	—
—	—	—	—	—	—	—	—	—	[1, 2]
56.05	55.67	70.46, 70.35	6.77, 6.93	69.90	6.79	162—163	14.32, 14.41	14.50	—



—	—	—	—	—	—	142—144	19.54, 19.59	19.86	[1, 8]
—	—	—	—	—	—	—	—	—	[8]
35.53	36.06	63.75, 63.92	10.49, 10.69	64.61	10.76	114—115	18.67, 18.47	18.06	—
—	—	—	—	—	—	—	—	—	[9]
—	—	—	—	—	—	143—145	17.27, 17.14	17.28	[1, 8]
—	—	—	—	—	—	—	—	—	[8]

On carrying out the same reaction with 2-butyn-1-ol acetate we actually were able to isolate acetic anhydride.

$$CH_3-C\equiv C-CH_2OCOCH_3 \xrightarrow[Hg(OCOCH_3)_2]{CH_3COOH} CH_3COCH_2CH_2OCOCH_3 + (CH_3CO)_2O$$

In the further course of the reaction the dimercuro compound (III) is cleaved by acetic acid to form mercuric acetate and methyl-β-hydroxyethyl ketone (IV). The latter is acetylated by the acetic anhydride (in presence of mercuric acetate) to the end product – methyl-β-acetoxyethyl ketone (V).

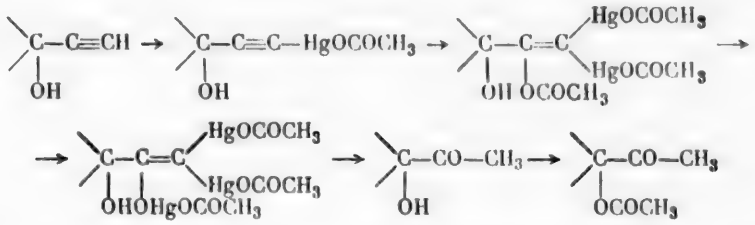
$$(III) \xrightarrow{CH_3COOH} \underset{(IV)}{CH_3COCH_2CH_2OH} \xrightarrow[Hg(OCOCH_3)_2]{(CH_3CO)_2O} \underset{(V)}{CH_3COCH_2CH_2OCOCH_3}$$

It should be pointed out that when tertiary acetylenic alcohols or 2-butyn-1-ol react with acetic acid in presence of mercuric acetate, the resulting acetoxy ketones are accompanied (in the lower boiling fraction) by a small quantity of free ketoalcohol.

It was shown in a special experiment that both methyl-β-hydroxyethyl ketone and dimethylacetylcarbinol are susceptible to acetylation by acetic anhydride in presence of mercuric acetate. It is known that the acetylenic hydrogen of monosubstituted acetylenic compounds is easily replaced by mercury on heating with mercury salts [4]. Since the carbon–mercury bond is strongly polarized, the polarization directivity of the triple bond (shift of the π-electron pair) in this case is strictly one-sided; consequently the site of subsequent addition of mercury salts is unequivocal.

$$-C\equiv CH + HgX_2 \longrightarrow -\overset{\delta+}{C}\equiv\overset{\delta-}{C}-HgX \xrightarrow{HgX_2} -\underset{X}{C}=C\begin{matrix}HgX\\HgX\end{matrix}$$

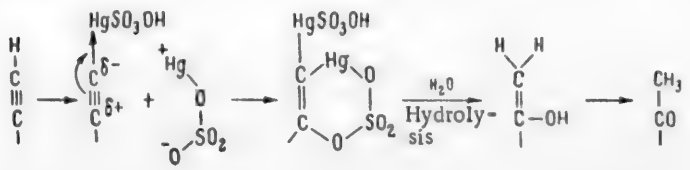
Thus, we can represent the mechanism of formation of acetates of acetylcarbinols from monosubstituted acetylenic alcohols on reaction with acetic acid in presence of mercuric acetate in the following manner:



All the resulting α-acetoxy ketones were hydrolyzed by aqueous alcoholic alkali to the corresponding α-ketoalcohols. The constants of the synthesized ketoalcohols and their acetates are set forth in the table.

For identification purposes the α-ketoalcohols described above were also prepared by the Kucherov method – by hydration of the corresponding acetylenic carbinols in aqueous alcoholic solutions in presence of mercuric sulfate. Monosubstituted acetylenic derivatives are usually hydrated selectively with formation exclusively of methyl ketones [10].

It is interesting to note that the earlier hypothesis about the mechanism and direction of hydration of disubstituted acetylenic compounds in presence of mercury salts [5] (mercuric sulfate) can also be extended to monosubstituted derivatives.



EXPERIMENTAL

Reaction of tertiary acetylenic carbinols with acetic acid in presence of mercuric acetate. A mixture of 0.1 mole of acetylenic carbinol, 35 g of glacial acetic acid and 1.5 g of mercuric acetate was refluxed for 6-8 hours. After the acetic acid had been removed (45° at 25 mm) the residue was twice fractionated in vacuo. All the resulting α-acetoxy ketones were hydrolyzed to the corresponding α-ketoalcohols by 10% aqueous alcoholic sodium hydroxide (see table).

Reaction of 2-butyn-1-ol with acetic acid in presence of mercuric acetate. A mixture of 7 g of 2-butyn-1-ol [6], 25 g of glacial acetic acid and 1 g of mercuric acetate was refluxed for 6 hours and the reaction mixture was fractionated in vacuo to give 0.5 g of methyl-β-hydroxyethyl ketone, with b. p. 70-73° (10 mm), $n^{20}D$ 1.4310, and 5.5 g of methyl-β-acetoxyethyl ketone with b. p. 80-82° (10 mm), $n^{20}D$ 1.4230. The semicarbazone of the latter melted at 135-136° and did not give a depression in admixture with an authentic sample [7].

Reaction of the acetate of 2-butyn-1-ol with acetic acid in presence of mercuric acetate. A mixture of 15 g of the acetate of 2-butyn-1-ol, 25 g of glacial acetic acid and 1.5 g of mercuric acetate was refluxed for 7 hours. The reaction mixture was fractionated in vacuo to give 12 g of methyl-β-acetoxyethyl ketone with b. p. 80-83° (10 mm), $n^{20}D$ 1.4235; the semicarbazone melted at 135-136° (from alcohol). The initial fraction (5 g) was twice fractionated at atmospheric pressure to give 3.5 g of acetic anhydride with b. p. 135-140°, $n^{20}D$ 1.4390; on heating with aniline it formed acetanilide with m. p. 115°.

Addition of mercuric acetate to the acetate of 2-butyn-1-ol. Into a solution of 3.2 g of mercuric acetate in 30 g of acetic acid at room temperature was stirred (dropwise) 1.2 g of the acetate of 2-butyn-1-ol in 5 g of acetic acid. The next day the reaction mixture was treated with saturated potassium chloride solution. The precipitate was washed with aqueous acetone. There was obtained 2 g of 1,3-diacetoxy-2-chloromercuributene-2 with m. p. 114-117° (in a sealed capillary).

Found %: Hg 49.58. $C_8H_{11}O_4ClHg$. Calculated %: Hg 49.26.

Reaction of ketoalcohols with acetic anhydride in presence of mercuric acetate. a) A mixture of 5 g of dimethylacetylcarbinol, 5 g of acetic anhydride, 15 g of acetic acid and 1 g of mercuric acetate was refluxed for 6 hours. Fractional distillation of the reaction mixture in vacuo gave 4.8 g of dimethylacetylcarbinol acetate with b. p. 60-63° (10 mm), $n^{20}D$ 1.4205; semicarbazone with m. p. 155-156° (no depression in mixed melting test) [1].

b) A mixture of 3 g of methyl-β-hydroxyethyl ketone, 3 g of acetic anhydride, 10 g of acetic acid and 0.7 g of mercuric acetate was refluxed for 3 hours. Fractional distillation in vacuo gave 2.5 g of methyl-β-acetoxyethyl ketone with b.p. 79-82° (10 mm), $n^{20}D$ 1.4235; the semicarbazone melted at 135° and did not give a depression in admixture with an authentic specimen.

SUMMARY

1. A convenient method was developed for preparation of acetates of α-acetylcarbinols by boiling acetic acid solutions of the corresponding acetylenic alcohols in presence of mercuric acetate.

2. It was shown that the disubstituted acetylenic alcohol, 2-butyn-1-ol, reacts with acetic acid in presence of mercuric acetate to give methyl-β-acetoxyethyl ketone.

3. A mechanism is proposed for the formation of acetoxy ketones by reaction of both monosubstituted and disubstituted acetylenic alcohols with acetic acid in presence of mercuric acetate.

LITERATURE CITED

1. I. N. Nazarov, Izvest. Akad. Nauk SSSR, Otdel. Tekh. Nauk 2, 215 (1940); I. N. Nazarov and T. D. Nagibina, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk 2, 303 (1941).
2. G. F. Hennion, J. Am. Chem. Soc. 62, 653 (1940).
3. É. D. Venus-Danilova and S. N. Danilov, Zhur. Obshch. Khim. 2, 644 (1932).

4. Synthetic Methods in the Field of Organometallic Compounds 3, 57, 74 (1945).
5. I. N. Nazarov and S. G. Matsoyan, Zhur. Obshch. Khim. 27, 2951 (1957);* S. G. Matsoyan, G. A. Chukhadzhyan, and S. A. Vartanyan, Zhur. Obshch. Khim. 29, 451 (1959).*
6. G. M. Mkryan, Izvest. Akad. Nauk Armen. SSSR, Seriya Tekh. Nauk 4, 79 (1947); 3, 259 (1948).
7. I. N. Nazarov, S. G. Matsoyan, and S. A. Vartanyan, Zhur. Obshch. Khim. 27, 1818 (1957).*
8. G. F. Hennion and Watson, J. Org. Chem. 23, 656 (1958).
9. W. J. Hickinbottom, A. A. Hyatt, and Sparke, J. Chem. Soc. (1954), p. 2529.
10. M. Kutcheroff, Ber. 14, 1540 (1881); 17, 13 (1884); K. Campbell and G. F. Hennion, J. Am. Chem. Soc. 60, 718 (1938); U. S. Patent 1,896,161 (1933); Chem. Abs. 27, 2458 (1933); H. Scheibler and Fischer, Ber. 55, 2903 (1922).

* Original Russian pagination. See C. B. translation.

ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

IX. ADDITION OF TRIALKYL PHOSPHITES TO α-DIKETONES

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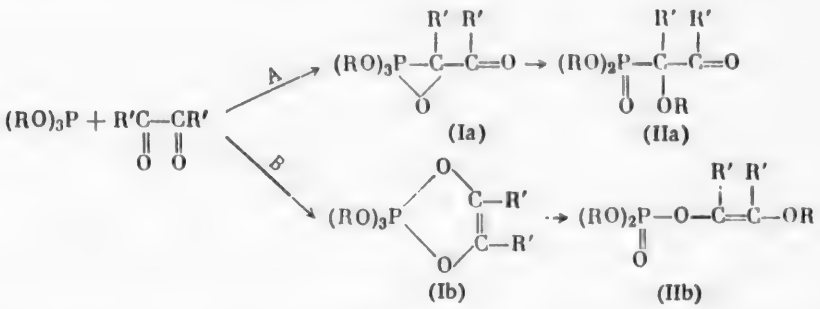
Kazan Branch of the Scientific Research Institute for Cinephotography
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1208-1216, April, 1960
Original article submitted May 11, 1959

In continuation of our investigations in the field of new forms of the Arbuzov rearrangement [1], we found that trialkyl phosphites react with very great facility with α-diketones. The reaction between diacetyl and trialkyl phosphites proceeds at room temperature with considerable evolution of heat. The study of these reactions revealed that, depending on the experimental conditions, we can obtain not only the end product of the Arbuzov rearrangement (II) but also the intermediate product of addition of trialkyl phosphite to diacetyl.

Reaction between trialkyl phosphites and α-diketones can proceed in theory in two directions (A and B), i.e., with or without transfer of the reaction center.



We concluded earlier [2] that route B is followed; but more careful study of the chemical and physicochemical properties of the reaction products showed that addition of trialkyl phosphites to α-diketones proceeds at one carbonyl group, i.e., according to route A. This is supported by the following facts.

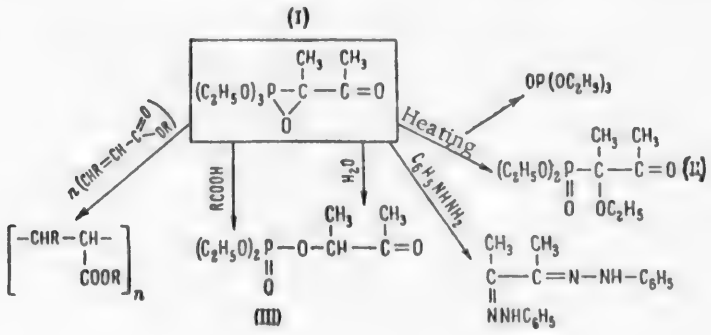
1. The final reaction product (II) (R = C_2H_5) is not in any circumstances transesterified by ethanol to triethyl phosphate, whereas the analogous β-chlorovinyl phosphates are easily transesterified to triethyl phosphate [3].

2. Hydrolysis of product (II) with barium hydroxide gives the barium salt of diethylphosphorous acid, whereas under the same conditions vinyldiethylphosphates form the barium salt of diethylphosphoric acid [4].

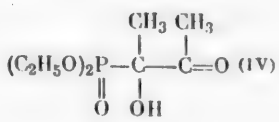
3. The Raman spectra of compounds (I) and (II), plotted at our request by B. A. Arbuzov and V. S. Vinogradova, do not contain double bond vibration frequencies; they contain strong lines at 1733 cm^{-1} (I) and 1728 cm^{-1} (II) which are close to the frequency of the vibrations of the carbonyl group.

We isolated intermediate products (I) ($R' = CH_3$; $R = C_2H_5$, C_3H_7, C_4H_9) in the chemically pure state and studied their properties (with reference to the product of addition of triethyl phosphate to diacetyl). In many respects the properties were similar to those of products of addition of trialkyl phosphites to α,β-unsaturated acids which we had earlier studied in the unpurified form [1].

Compound (I) reacts vigorously with water to form (III). This reaction even takes place with moisture of the air.



Reaction of (I) with water may be expected to lead to the ester of α-hydroxyalkylphosphinic acid.



However the compound that we obtained from (I) was not identical with the product (IV) previously described by Abramov, Belokon' and Makhmutova [5].

Saponification of (III) with aqueous barium hydroxide gave the barium salt of diethyl phosphate. The infrared spectrum of this substance does not contain absorption bands of the hydroxy group in the 3200-3300 cm^{-1} region which are characteristic of α-hydroxyalkylphosphinic esters [8]. All these data support the conclusion that product (II) is diethyl-(α, β-dimethyl-β-ketoethyl)-phosphate. Intermediate product (I) very quickly changes its physical properties on standing in the air and is converted mainly into triethyl phosphate and product (III). Heating in solution in ether and other solvents converts it mainly into triethyl phosphate and into diethyl-(α,β-dimethyl-β-ketoethyl)-phosphate (III). It can be kept unchanged for a considerable period at room temperature when out of contact with the air (in a sealed ampoule). Heating in a sealed ampoule converts it partly into end product (II) (ethyl ester of α-ethoxy-α,β-dimethyl-β-ketoethylphosphinic acid) and partly into triethyl phosphate.

We studied the influence of experimental conditions (temperature, solvents, catalysts) on the course of the second step of the Arbuzov rearrangement in this reaction. Results of the main experiments are presented in Table 2. These investigations show that pure (I), out of contact with air, is converted with difficulty into end product (II), the reaction being complicated by formation of triethyl phosphate and by resinification of the product at higher temperatures. Conversion of compound (I) is accelerated in acetone and alcohol; in the latter solvent the yield of triethyl phosphate is considerably increased. Triethyl phosphite and end product (II) do not accelerate the conversion proceeding according to the second step of the Arbuzov rearrangement. Isomerization of the intermediate product is greatly accelerated by diacetyl; addition of an alkyl halide also speeds up the second step of the reaction. Ultraviolet irradiation does not speed up isomerization of the intermediate product.

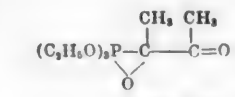
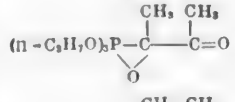
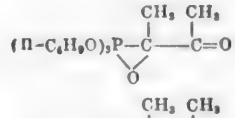
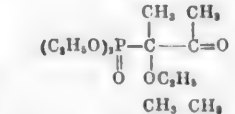
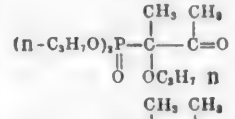
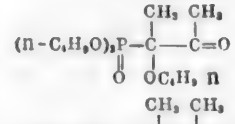
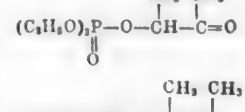
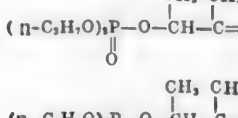
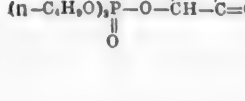
We were also interested in establishing whether end product (II) intensifies the catalytic action of diacetyl on the reaction course. Experiments showed that simultaneous addition of these two substances does not speed up the reaction more than diacetyl alone; the yield of triethyl phosphate increases slightly. It must be pointed out that stepwise operation of the reaction gives a lower yield of end product than direct preparation from diacetyl and trialkyl phosphite.

Organic acids react very energetically with substance (I) and convert it into (III). Product (I) is a very active initiator of the polymerization of methacrylic acid and methyl methacrylate. Addition of catalytic quantities of product (I) to methacrylic acid causes rapid polymerization at room temperature. A special experiment established that polymerization is initiated only in presence of air; polymerization does not take place when product (I) is added to methacrylic acid in a sealed U-shaped ampoule under vacuum.

Compounds (I) and (II) react with phenylhydrazine to give diacetyl diphenylhydrazone in quantitative yield. We were unable to establish the fate of the phosphoric portion of the molecule in this reaction.

Reaction between benzil and trialkyl phosphites is less violent. The first step gives an intermediate product analogous to the product of addition to diacetyl. It could not, however, be isolated in the pure form. During fractionation it breaks down with liberation of benzil. Its properties were studied in the impure form. Like the intermediate product of addition to diacetyl, it reacts with water very energetically and initiates polymerization.

TABLE 1

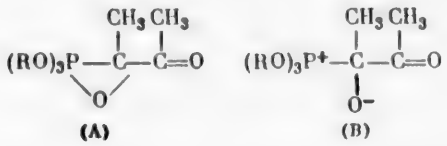
Number	Formula	Boiling point (pressure in mm)	n_D^{20}	d_0^{20}	P % found	P % calc.	Yield (in %)
1		104—105° (10)	1.4290	1.0825	12.42	12.30	72.0
2		127—130 (10)	1.4305	1.0256	10.92	10.51	31.5
3		138—140 (10)	1.4335	0.9977	10.65	9.63	30.2
4		127—130 (10)	1.4250	1.1061	12.32	12.30	23.4
5		140—142 (10)	1.4230	1.0752	11.17	10.51	10.4
6		148—150 (10)	1.4240	1.0192	9.83	9.63	46.8
7		132—134 (10)	1.4210	1.1122	13.78	13.84	70.1
8		148—150 (10)	1.4220	1.0432	12.21	12.31	68.2
9		158—162 (10)	1.4260	1.0120	11.58	11.08	69 4

Its constants alter with prolonged heating and the properties inherent to the intermediate product disappear; however, it was impossible to distill the end product of the reaction or the product of the action of water on the intermediate product even in high vacuum (1×10^{-3} mm). In an earlier communication [6] we described the reaction of trialkyl phosphites with pyruvic acid which led to formation of trialkyl phosphates.

$$(RO)_3P + CH_3COCOOH \rightarrow (RO)_3P{=}O$$

Pyruvic acid resembles α-diketones in possessing an O=C−C=O conjugated system. We therefore made attempts to obtain more interesting products by this reaction. We were unable, however, to obtain products other than triethyl phosphate even by operation at − 30 to −10° in an inert atmosphere. The physical constants of the resulting products are set forth in Table 1.

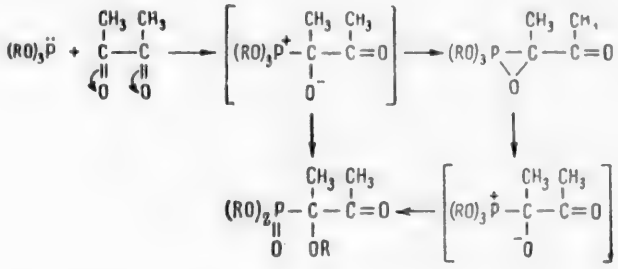
Regarding the structure of the intermediate products of the Arbuzov rearrangement that we prepared, it seems to us more probable that they contain pentacovalent phosphorus (A) and not a phosphonium grouping (B).



(A) (B)

Unlike ionic compounds, they do not crystallize even after deep freezing, and they distill without decomposition. They are soluble in nonpolar organic solvents. Like pentaphenylphosphorus, they initiate polymerization of unsaturated compounds. Water and acids rupture the P−C bond without addition of a proton to the oxygen.

Like phosphinemethylenes they can probably ionize during the reaction. In that event the mechanism of the Arbuzov rearrangement can be represented in the following way:



If we assume that conversion of intermediate product to end product involves an ionization step, then we are forced to the conclusion that the bipolar ion initially formed by addition of trialkyl phosphate to diacetyl can spontaneously change into the end product with omission of the intermediate step. This process evidently proceeds concurrently with formation of intermediate product, whereas stepwise operation of the reaction is complicated by secondary processes.

EXPERIMENTAL

Addition of triethyl phosphite to diacetyl. Experiment 1. To an ethereal solution of 30 g of triethyl phosphite was slowly added (dropwise) 15.7 g of diacetyl. The temperature rose to 38° and further temperature rise was prevented by ice water cooling of the flask. The reaction mass was stood at room temperature until the next day. Vacuum distillation gave 30.2 g (72%) of intermediate product (I).

B. p. 104-105° (10 mm), $n^{20}D$ 1.4290, d^{20}_0 1.0825.

Found %: P 12.42. $C_{10}H_{21}O_5P$. Calculated %: P 12.30.

In addition, 8 g (28%) of triethyl phosphate was obtained; b. p. 92-95° (9 mm), $n^{20}D$ 1.4050, d^{20}_0 1.0691.

Experiment 2. Dropwise addition of 50 g of triethyl phosphite was made to 25 g of diacetyl. The temperature of the mixture quickly rose to 60-80°. After the phosphite had been added, the reaction mass was heated for 10 hours on a water bath. Vacuum distillation gave the following fractions: 1st, 15.8 g (24.2%) of triethyl phosphate; 2nd, 10.4 g (13.3%) of intermediate product (I). (Constants identical with those in Expt. 1); 3rd, 23.4 g (30.4%) of diethyl ester of α-ethoxy-α, β-dimethyl-β-ketoethylphosphinic acid.

B. p. 127-130° (10 mm), $n^{20}D$ 1.4250, d^{20}_0 1.1061.

Found %: P 12.32. $C_{10}H_{21}O_5P$. Calculated %: P 12.30.

About 20 experiments in all on preparation of compounds (I) and (II) were carried out under various conditions. Both products were formed in different ratios in the majority of experiments.

Addition of tripropyl phosphite to diacetyl. Diacetyl (16.6 g) was slowly added dropwise to an ethereal solution of tripropyl phosphite (40 g). The reaction was strongly exothermic and the flask was externally cooled with ice-water. The reaction mass was stood overnight at room temperature. Vacuum distillation gave: 1) 10 g (23.3%) of tripropyl phosphate with b. p. 120-124° (10 mm), d^{20}_0 1.0072.

Found %: P 13.72. $C_9H_{21}O_4P$. Calculated %: P 13.83.

2) 31.5 g (55.2%) of intermediate product (I) with b. p. 127-130° (10 mm), $n^{20}D$ 1.4305, d^{20}_0 1.0256.

Found %: P 10.92. $C_{13}H_{27}O_5P$. Calculated %: P 10.51.

3) 6 g (10.4%) of dipropyl ester of α-propoxy-α,β-dimethyl-β-ketoethylphosphinic acid, b. p. 148-150° (12 mm), $n^{20}D$ 1.4230, d^{20}_0 1.0752.

Found %: P 11.17. $C_{13}H_{27}O_5P$. Calculated %: P 10.51.

Addition of tri-n-butyl phosphite to diacetyl. Dropwise addition of 13.7 g of diacetyl was made to an ethereal solution of 40 g of tri-n-butyl phosphite. Vacuum distillation gave: 1) 15.2 g (30.2%) of intermediate product (I) with b. p. 138-140° (10 mm), $n^{20}D$ 1.4335, d^{20}_0 0.9977.

Found %: P 10.65. $C_{16}H_{33}O_5P$. Calculated %: P 9.63.

The high value found for phosphorus was due to contamination with the low-boiling tributyl phosphate. Complete purification was impossible.

2) 21.7 g (46.8%) of dibutyl ester of α-butoxy-α,β-dimethyl-β-ketoethylphosphinic acid, b. p. 148-150° (10 mm), $n^{20}D$ 1.4240, d^{20}_0 1.0192.

Found %: P 9.83. $C_{16}H_{33}O_5P$. Calculated %: P 9.63.

These experiments likewise were repeated many times under various conditions.

Action of water on intermediate product (I). To 20 g of intermediate product (I), obtained by reaction of triethyl phosphite with diacetyl, was added 1.4 g of water. An emulsion was formed and rapidly dissolved on vigorous shaking with considerable release of heat. The temperature rose to 98°. After the reaction mixture had cooled to room temperature, the low-boiling products were distilled off at normal pressure. This operation gave 2.7 g (75%) of ethyl alcohol. Further distillation in vacuo gave 12.5 g (70.1%) of diethyl-α,β-dimethyl-β-ketoethyl-phosphate with b. p. 132-133° (10 mm), $n^{20}D$ 1.4210, d^{20}_0 1.1122.

Found %: P 13.82. $C_8H_{17}O_5P$. Calculated %: P 13.83.

The other intermediate products were similarly reacted with water.

Action of acetic acid on intermediate product (I). To 15 g of (I), prepared from triethyl phosphite and diacetyl, was added 3.6 g of glacial acetic acid. The reaction was strongly exothermic and the temperature rose by 74°. After cooling of the reaction mass to room temperature, the volatile products were distilled off to give 2.5 g (60%) of ethyl acetate (b. p. 72-76°, $n^{20}D$ 1.3705). Vacuum distillation gave 8 g (61.5%) of diethyl-(α,β-dimethyl-β-ketoethyl)-phosphate with b. p. 130-132° (10 mm), $n^{20}D$ 1.4210.

Found %: P 13.74. $C_8H_{17}O_3P$. Calculated %: P 13.83.

Hydrolysis of diethyl-(α,β-dimethyl-β-ketoethyl)-phosphate. To 5 g of the diethyl ester was added an aqueous solution of 5 g of barium hydroxide. The temperature rose by 7°. The reaction mixture was refluxed for 8 hours. After completion of reaction, the mass was saturated with carbon dioxide to bind unreacted barium hydroxide. The barium carbonate was separated and the filtrate evaporated. The residual barium salt was washed with alcohol and dried. Amount of barium salt 4.8 g.

Found %: P 13.87, 13.67; Ba 30.67, 30.82. $C_8H_{20}O_8P_2Ba$. Calculated %: P 13.97; Ba 30.72.

Hydrolysis of diethyl ester of α-ethoxy-α,β-dimethyl-β-ketoethylphosphinic acid. To 5 g of the diethyl ester was added an aqueous solution of 5 g of barium hydroxide. The temperature rose by 5°. The reaction mixture was refluxed for 8 hours. The mass was then saturated with carbon dioxide to bind unreacted barium hydroxide. The filtrate from the precipitated $BaCO_3$ was evaporated and the residual barium salt washed with alcohol and dried. Yield of salt 3.8 g.

Found %: P 14.81, 14.87. $C_8H_{20}O_6P_2Ba$. Calculated %: P 15.03.

Action of phenylhydrazine on compounds (I) and (II). To an ethereal solution of 12 g of intermediate product (I), obtained by reaction of triethyl phosphite with diacetyl, was added (dropwise) an ethereal solution of 10 g of phenylhydrazine. There was obtained 8.5 g (77%) of diacetyl diphenylhydrazone. After three recrystallizations from alcohol the diphenylhydrazone had m. p. 240-242°. Literature data: m. p. 243-244° [7].

Found %: C 72.20; H 6.96. $C_{16}H_{18}N_4$. Calculated %: C 72.30; H 6.77.

Phenylhydrazine was similarly reacted with the diethyl ether of α-ethoxy-α, β-dimethyl-β-ketoethylphosphinic acid (II). The product of the reaction was again diacetyl diphenylhydrazone.

TABLE 2

No.	Experimental conditions: temp.	reaction duration (hr)	solvent	catalyst, wt., %	Yield of product (I)	Yield of triethylphosphate	Residue of unreacted product (I)	Remarks
1	90°	25	Acetone	—	21.0	15.0	50.0	*
2	90	25	Alcohol	—	20.1	44.6	24.6	*
3	90	25	—	Diacetyl (5)	23.0	—	63.0	*
4	90	25	—	Diacetyl (6)	13.6	20.0	42.5	**
5	90	25	—	(II) (1)	8.0	—	52.0	*
6	90	25	—	—	6.0	18.0	54.0	*
7	90	25	—	Triethylphosphite (1)	—	—	84.2	*
8	90	25	Pyridine	—	12.0	38.2	40.0	**
9	90	25	Nitrobenzene	—	4.0	***	21.0	**
10	37	25	Ether	—	—	13.3	40.0	** Product (III) obtained in 46.1% yield
11	40	25	Ether	Diacetyl (3.5)	20.0	27.0	25.0	**
12	90	5		Ultraviolet irradiation	—	15.0	81.6	*In a nitrogen atmosphere
13	90	5	—	-	—	—	89.0	*In a nitrogen atmosphere
14	Room temperature	25 (in air)	—	—	—	42.0	27.0	Product (III) obtained in 13% yield

* Experiments in a sealed ampoule.

** Experiments in a flask under a reflux condenser.

*** The triethyl phosphate was not separated from the nitrobenzene due to the closeness of their boiling points.

Polymerization of acrylates in presence of intermediate product (I). a) Polymerization in the air. To 5 g of methacrylic acid was added 0.01 g of intermediate product (I). The acid began to polymerize after a few seconds and 4.6 g of polymeric methacrylic acid was obtained in the form of a white solid, poorly soluble in organic solvents.

b) Polymerization with exclusion of air. Polymerization was carried out in a special U-shaped vessel. In one limb was placed 5 g of methacrylic acid and in the other 0.01 g of intermediate product (I). The air was pumped out and the container sealed under vacuum. After 5 days the contents were mixed. Polymerization did not take place even after standing for five days.

Isomerization of product (I). Isomerization was carried out by heating the intermediate product obtained from triethyl phosphite and diacetyl under various conditions in presence of various solvents and additives in a sealed ampoule or in a flask connected to a reflux condenser topped by a calcium chloride tube. Results of the principal experiments are set forth in Table 2. Most of the experiments were repeated many times.

Interaction of triethyl phosphite with benzil. Triethyl phosphite (15 g) was added dropwise to an ethereal solution of benzil (18.9 g). Spontaneous heating was observed within a short time after the whole quantity of triethyl phosphite had been added, the temperature rising to 38°. The reaction mixture was heated for 4 hours on a water bath. A qualitative test for triethyl phosphite with a copper halide gave a negative result. The ether was taken off in vacuo. The crude product initiated polymerization of methacrylic acid. It reacted with water with a 25° rise of temperature. Attempts to fractionate the addition product were unsuccessful, the product breaking down with formation of triethyl phosphate and benzil.

The intermediate product (10 g) was heated for 20 hours at 80-90° under a reflux condenser topped by a calcium chloride tube. The properties characterizing the intermediate reaction product gradually disappeared. Attempts to fractionate the reaction products in high vacuum (1×10^{-3} mm) were unsuccessful. Decomposition took place with formation of benzil and triethyl phosphate.

Interaction of triethyl phosphite with pyruvic acid. Addition of pyruvic acid (10.6 g) to an ethereal solution of triethyl phosphite (cooled to − 30°) was effected slowly (dropwise) in a carbon dioxide atmosphere. During the operation the temperature rose to − 10°. After completion of the dropwise addition, the ether was taken off in a carbon dioxide atmosphere. Fractionation was effected in vacuo and gave 14 g (62.7 %) of triethyl phosphate with b. p. 92-95° (10 mm), $n^{20}D$ 1.4065.

SUMMARY

1. The interaction of trialkyl phosphites with α-diketones was studied. Intermediate products of this Arbuzov rearrangement reaction were isolated.

2. A study was made of some properties of the intermediate products and of the influence of various factors on the course of the second step of the Arbuzov rearrangement.

LITERATURE CITED

1. V. A. Kukhtin and A. N. Pudovik, Uspekh. Khim. 28, 91 (1959).
2. V. A. Kukhtin, Doklady Akad. Nauk SSSR 121, 426 (1958).*
3. A. N. Pudovik, Doklady Akad. Nauk SSSR 105, 735 (1955).
4. N. Kreutzkamp and H. Kayser, Lieb. Ann. 609, 39 (1957).
5. V. S. Abramov, L. Sh. Belokon', and F. I. Makhmutova, Zhur. Obshch. Khim. 28, 665 (1958).*
6. Gil'm Kamai and V. A. Kukhtin, Trudy Kazan. Khim.-Tekh. Inst. 23, 133 (1957).
7. Dictionary of Organic Compounds [Russian translation] (IL, 1949), Vol. 1, p. 627.
8. C. Miller, R. Miller, and W. Rogers, J. Am. Chem. Soc. 80, 1562 (1958).

* Original Russian pagination. See C. B. translation.

PRODUCTS OF BROMINATION OF 2,4-DINITROPHENYLACETONE

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We required a supply of 1-bromo-3-(2,4-dinitrophenyl)-2-propanone (I) as starting material for synthetic investigations.

According to the literature [1], two substances appear to be formed during bromination of 2,4-dinitrophenylacetone. One of these was apparently 1-bromo-3-(2,4-dinitrophenyl)-2-propanone. The authors established that in both substances the bromine was in the side chain but it was not established which of them was 1-substituted.

We also obtained, depending on the conditions, two bromoketones of the same composition by bromination of 2,4-dinitrophenylacetone [2] in glacial acetic acid. One of them, m.p. 96-97° (I), is formed by bromination of 2,4-dinitrophenylacetone at 50-60°; the other, with m. p. 115-116°, is formed at 13-15° (II).

We synthesized 1-bromo-3-(2,4-dinitrophenyl)-2-propanone from 2,4-dinitrophenylacetic acid with the aim of establishing the structures of the two compounds. We prepared 2,4-dinitrophenylacetyl chloride, reacted it with diazomethane to give a diazoketone not previously described in the literature, and reacted the latter with hydrogen bromide to give 1-bromo-3-(2,4-dinitrophenyl)-2-propanone with m. p. 96-97°. This was identical with bromoketone (I) prepared from 2,4-dinitrophenylacetone. Consequently, bromoketone (II) with m. p. 115-116° is 3-bromo-3-(2,4-dinitrophenyl)-2-propanone. This result of our investigation is consistent with A. E. Favorskii's observation that bromination of ketones leads to preferential substitution of a hydrogen at the less hydrogenated carbon atom [3]. We noted that 24-hours' standing of the reaction mass containing bromoketone (II) at room temperature led to formation of the substance with m. p. 96-97°. We also effected conversion of (II) into (I) by boiling in glacial acetic acid in presence of hydrogen bromide.

In this manner, we detected yet another example of anionotropic rearrangement of unsymmetrical α-haloketones which was earlier investigated for halogen-substituted β-ketoesters, β-diketones and steroids [4], and more recently described [5, 6] for the simplest α-bromoketones.

EXPERIMENTAL

Bromination of 2,4-dinitrophenylacetone. a) In the course of 15 minutes a solution of 1.7 g of bromine in 3.8 ml of glacial acetic acid was added to a solution of 2.5 g of 2,4-dinitrophenylacetone in 10 ml of glacial acetic acid at 55-60°. The mixture was kept at this temperature for 15 minutes and then left at room temperature until the next day. The resulting crystals of bromoketone (I) were filtered off; 0.75 g, m. p. 93-94°. The acetic acid solution was run into water and deposited a further 1.85 g of substance with m. p. 90-91°. After recrystallization from a mixture of alcohol and ether, 1-bromo-3-(2,4-dinitrophenyl)-2-propanone (I) formed colorless crystals with m. p. 96-97°.

Found %: Br 26.05; N 9.02. $C_9H_7O_5N_2Br$. Calculated %: Br 26.37; N 9.25.

b) In the course of 15 minutes a solution of 1.7 g of bromine in 3.8 ml of glacial acetic acid was stirred into a solution of 2.5 g of 2,4-dinitrophenylacetone in 10 ml of glacial acetic acid at 12-15°. Crystals began

to come down after about 1 hour 40 minutes. Five minutes after start of crystallization, the crystals were filtered off, washed with ether and dried. There was obtained 1.3 g of substance with m. p. 114-115°. The acetic acid mother liquor was quickly run into water and then deposited a further 1.3 g of substance with m. p. 107-114°. After recrystallization from a mixture of alcohol and ether, 3-bromo-3-(2,4-dinitrophenyl)-2-propanone (II) formed colorless crystals with m. p. 115-116°.

Found %: Br 26.65; N 9.03. $C_9H_7O_5N_2Br$. Calculated %: Br 26.37; N 9.25.

Rearrangement. A suspension of 0.3 g of bromoketone (II), m. p. 115-116°, in 3 ml of glacial acetic acid was boiled with five drops of hydrobromic acid for 0.5 hour. The mass was poured into a mixture of water and ice. After recrystallization, the product had m. p. 96-97° and did not give a depression of melting point in admixture with bromoketone (I).

2,4-Dinitrobenzil diazomethyl ketone. To a solution of diazomethane in 90 ml of ether (prepared from 7.5 g of nitrosomethylurea at − 2°) was gradually added a solution of 4.65 g of 2,4-dinitrophenylacetyl chloride [7] in 100 ml of absolute ether. The mixture was left until the next day in a refrigerator, and the crystalline precipitate (2.9 g) was filtered, washed with a little cold ether, and recrystallized from methanol. M. p. 112 to 113°.

Found %: C 43.77; H 2.64. $C_9H_6O_5N_4$. Calculated %: C 43.24; H 2.42.

1-Bromo-3-(2,4-dinitrophenyl)-2-propanone (I). To a suspension of 2.6 g of 2,4-dinitrobenzil diazomethyl ketone in 26 ml of methanol at room temperature was added dropwise 3.5 ml of 40% hydrobromic acid. The mixture was boiled until bubbles of nitrogen ceased to come off. A precipitate came down on cooling and was filtered and dried. There was obtained 2 g of 1-bromo-3-(2,4-dinitrophenyl)-2-propanone with m. p. 95-96°; no depression of melting point in admixture with bromoketone (I).

SUMMARY

1. Bromination of 2,4-dinitrophenylacetone gave, depending on the conditions, either 1-bromo-3-(2,4-dinitrophenyl)-2-propanone or 3-bromo-3-(2,4-dinitrophenyl)-2-propanone. 3-Bromo-3-(2,4-dinitrophenyl)-2-propanone is transformed into its isomer on heating in glacial acetic acid in presence of hydrobromic acid.

2. The structure of 1-bromo-3-(2,4-dinitrophenyl)-2-propanone was confirmed by its preparation from 2,4-dinitrophenylacetic acid via the diazoketone.

LITERATURE CITED

1. P. W. Neber and A. Burgard, Lieb. Ann. 493, 292 (1932).
2. W. Borsche, Ber. 42, 602 (1909).
3. A. E. Favorskii, J. pr. Chem. 88, 641 (1913).
4. M. S. Kharasch, E. Sternfeld, and E. R. Mayo, J. Am. Chem. Soc. 59, 1655 (1937); A. Hantzsch, Ber. 27, 3168 (1894).
5. A. C. Smith, W. Wilson, and R. Woodger, Chemistry and Industry 41, 309 (1954).
6. C. L. Stevens and C. T. Lenk, J. Org. Chem. 19, 538 (1954).
7. W. Borsche, Lieb. Ann. 390, 27 (1912).

INTRODUCTION OF SUBSTITUENTS INTO THE BENZENE RING OF INDOLE

VI. SYNTHESIS OF SULFO DERIVATIVES OF INDOLE AND INDOLINE [1]

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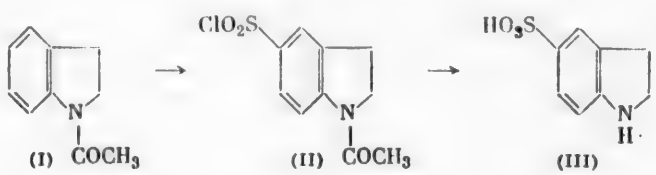
Indoles containing a sulfo or sulfamido group in the benzene ring were previously obtained by the Fischer reaction from corresponding substituted phenylhydrazines [2-5]. An extremely complicated synthesis of amides and esters of 3-carbethoxy-5-indolesulfonic acids from 3,4-quinoline-quinone diazides, involving many steps, was later described [6]. However, these methods did not give sulfo derivatives of indole not containing substituents in the benzene ring.

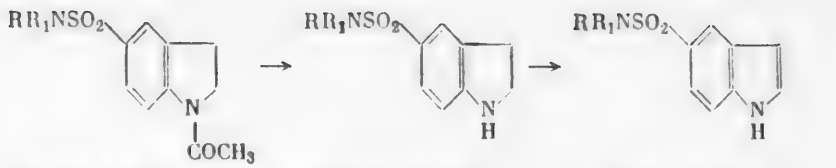
In the present work we describe a synthesis of 5-indolesulfamides by dehydrogenation of the corresponding 5-indolinesulfamides; the latter were prepared from indolinesulfochloride. Sulfochlorination of indolines and their closest analogs – tetrahydroquinolines – has not previously been described. We showed that 1-acetylindoline (I) reacts with chlorosulfonic acid to form 1-acetylindoline-5-sulfochloride (II). The reaction was conducted under the same conditions as for preparation of p-acetaminobenzenesulfochloride [7]. Hydrolysis of sulfochloride (II) with hydrochloric acid gives 5-indolinesulfonic acid (III).



(I) (II) (III)

The position of the sulfo group was confirmed by detection of the $SO_4^{=}$ in solution after acid (III) had been reacted in the cold with bromine water. It is well known that under mild conditions bromine only displaces the sulfo group in the para-position to the amino group in the benzene ring [8, 9].

Heating of sulfochloride (II) with ammonium carbonate gave 1-acetylindoline-5-sulfonamide (IV). N,N-Dimethylamide of 1-acetylindoline-5-sulfonic acid (V) was obtained by reaction of (II) with aqueous dimethylamine (67.2%), and N-methyl-N-phenylamide of 1-acetylindoline-5-sulfonic acid (VI) by heating of (II) with methylamine and sodium bicarbonate. Hydrolysis with hydrochloric acid converted these 1-acetylindolinesulfamides (IV, V, VI) into the corresponding indolinesulfamides (VII, VIII, IX). In the case of (VI) the S – N bond was partly hydrolyzed since methylaniline was detected in addition to the methyl-N-phenylamide of 5-indolinesulfonic acid (IX).



(IV) R = R$_1$ = H, (V) R = R$_1$ = CH$_3$, (VI) R = CH$_3$, R$_1$ = C$_6$H$_5$. (VII) R = R$_1$ = H, (VIII) R = R$_1$ = CH$_3$, (IX) R = CH$_3$, R$_1$ = C$_6$H$_5$. (X) R = R$_1$ = H, (XI) R = R$_1$ = CH$_3$, (XII) R = CH$_3$, R$_1$ = C$_6$H$_5$.

Heating of the indolinesulfamides with chloranil in xylene converted them into the corresponding indolesulfamides. The following total yields of indolesulfamides, calculated on the unsubstituted indole, were obtained (in %): (X), amide of 5-indolesulfonic acid 13.7; (XI), N,N-dimethylamide of 5-indolesulfonic acid 18; (XII), N-methyl-N-phenylamide of 5-indolesulfonic acid 9.8.

It is interesting to note that the formal analog of 1-acetylindoline – N-acetyl-o-toluidine – forms 2-acetamino-4-toluenesulfochloride on sulfochlorination, i.e., the SO_2Cl group enters in the meta-position to the acetylamino group [10]. Comparison of the behavior of indolines and o-toluidines in electrophilic substitution reactions shows that, in spite of the outward similarity, these compounds differ in their behavior in many substitution reactions. Thus, N,N-dimethyl-o-toluidine does not undergo nitrosation by sodium nitrite in hydrochloric acid [12], while N-methylindoline couples with diazotized sulfanilic acid in the 5 position and also forms a 5-nitroso derivative when treated with nitrous acid [13]. N-Methyl-N-acetyl-o-toluidine is nitrated in the meta-position to the methylacetamino group [11], while N-acetylindoline is nitrated in the para-position (the 5-position) [14]. Friedel--Crafts acylation of N-acetylindolines results in replacement of the hydrogen in the para-position to the acetamino group [1], whereas N-acetyl-o-toluidine under the same conditions forms meta-derivatives (relative to the acetamino group) [15].

The difference in behavior of analogous open and closed systems may be accounted for by the following considerations. In the case of N,N-disubstituted o-toluidine the CH_3 and NR_2 groups cannot, owing to steric hindrance, lie in the plane of the benzene ring. Consequently the axes of the clouds of p-electrons of the nitrogen and the π-electrons of the benzene ring are no longer parallel, and therefore the conjugation of the NR_2 group with the benzene ring is upset. Hence in disubstituted o-toluidines, electrophilic substitution reactions are directed to the para-position to the methyl group [16, 17]. Due to formation of a ring, the indoline molecule is coplanar, and the conjugation of the p-electrons of the nitrogen with the π-electrons of the benzene ring is not violated. Hence electrophilic substitution reactions take effect in the para-position to the amino group which is the stronger orienting influence.

Again, the conjugation of the NR group with the benzene ring is evidently not violated in tetrahydroquinoline and its N-derivatives, and in the majority of cases the orientation in the indoline series is the same as in the tetrahydroquinoline series. An exception arises in the nitration of N-acetyltetrahydroquinoline when a mixture of para- and meta-isomers (relative to the amino group) is formed [18]. As already indicated, 1-acetylindolines undergo nitration in the para-position to the amino group. The different direction of nitration in this case may be associated with the differing influences of the five- and six-membered ring on the benzene ring. It is known, for example, that derivatives of indane and tetralin manifest different orientations in some substitution reactions (the Mills – Nixon effect) [17]. This phenomenon has not previously been satisfactorily explained.

EXPERIMENTAL

1-Acetylindoline-5-sulfochloride (II). 1-Acetylindoline (I) (23 g) was added in small portions with intensive stirring and water cooling to 60 ml of chlorosulfonic acid. Slight heat was developed and hydrogen chloride was evolved violently. After the whole of the 1-acetylindoline had been added, the reaction mixture was heated on a water bath for 1.5 hours at 50-60° and then poured onto ice with vigorous stirring. There was obtained 20 g (54%) of 1-acetylindoline-5-sulfochloride; colorless crystals with m. p. 170-171° (from octane).

Found %: C 46.10; H 3.80. $C_{10}H_{10}O_3NSCl$. Calculated %: C 46.24; H 3.88.

5-Indolinesulfonic acid (III) was prepared by boiling 15.5 g of 1-acetylindoline-5-sulfochloride (II) with hydrochloric acid. The solution was evaporated to dryness on a water bath and the residue recrystallized from methanol to give crystals that decomposed when heated to above 300°. Good solubility in water.

Found %: N 6.79; S 16.07. $C_8H_9O_3NS$. Calculated %: N 7.04; S 16.09.

To a solution of analytically pure 5-indolinesulfonic acid (1.12 g) was added, dropwise with stirring, bromine water containing 1.8 g of bromine. The color of bromine disappeared quickly. Addition of barium chloride solution brought down a precipitate insoluble in hydrochloric acid (barium sulfate).

Amide of 1-acetylindoline-5-sulfonic acid (IV). A mixture of 7.8 g of 1-acetylindoline-5-sulfochloride (II) and 28 g of ammonium carbonate was pulverized in a mortar and placed in a flask which was then heated for 2 hours on a boiling water bath. The reaction mass was treated with water. There was obtained 4.9 g (68%) of the amide of 1-acetylindoline-5-sulfonic acid. Colorless crystals, soluble in hot water and caustic alkali. M. p. 223-224° (from aqueous alcohol).

Found %: C 50.27; H 5.24; N 11.47. $C_{10}H_{12}O_3N_2S$. Calculated %: C 49.98; H 5.04; N 11.65.

N,N-Dimethylamide of 1-acetylindoline-5-sulfonic acid (V). Finely pulverized 1-acetylindoline-5-sulfonic acid (II) (4.6 g) was stirred with 100 ml of 28% dimethylamine solution. Crystals were filtered off after 2 hours. M. p. 188.5-189.5° (from alcohol).

Found %: N 10.27. $C_{12}H_{16}O_3N_2S$. Calculated %: N 10.44.

N-Methyl-N-phenylamide of 1-acetylindoline-5-sulfonic acid (VI). Into 5.8 g of 1-acetylindoline-5-sulfochloride (II) was stirred 7 ml of methylaniline followed by a solution of sodium bicarbonate. The mixture was heated on a water bath, cooled and acidified with hydrochloric acid. There was obtained 7.2 g of (VI) which was recrystallized from alcohol to give 4.7 g (63.5%) of product in the form of colorless crystals with m. p. 179.5 to 180.5°.

Found %: N 8.30. $C_{17}H_{18}O_3N_2S$. Calculated %: N 8.48.

5-Indolinesulfonamide (VII). Obtained by boiling of the amide of 1-acetylindoline-5-sulfonic acid (IV) (0.75 g) with hydrochloric acid (1 :1) for an hour followed by addition of sodium bicarbonate. Yield 0.45 g (72.7%). Colorless crystals. M. p. 161-162° (from water).

Found %: C 48.07; H 4.95; S 16.20. $C_8H_{10}O_2N_2S$. Calculated %: C 48.45; H 5.09; S 16.17.

N,N-Dimethylamide of 5-indolinesulfonic acid (VIII) was prepared in a yield of 93.4% by hydrolysis of the N,N-dimethylamide (V). M. p. 108.5-109° (from water).

Found %: N 12.23. $C_{10}H_{14}O_2N_2S$. Calculated %: N 12.38.

N-Methyl-N-phenylamide of 5-indolinesulfonic acid (IX). Prepared by hydrolysis in dilute hydrochloric acid of 1 g of acetyl derivative (VI). After addition of sodium bicarbonate to the acid solution, the hydrolysis product was extracted with ether, the ether was evaporated and the viscous mass (strongly smelling of methylaniline) was recrystallized from aqueous methanol. There was obtained 0.4 g of colorless crystals of N-methyl-N-phenylamide of 5-indolinesulfonic acid. Purified for analysis by recrystallization from carbon-containing alcohol. M. p. 87.5-88°.

Found %: N 9.57. $C_{15}H_{16}O_2N_2S$. Calculated %: N 9.71.

5-Indolesulfonamide (X). A suspension of 2.3 g of amide (VII) and 2.86 g of chloranil in 100 ml of xylene was heated at the boil for 4 hours. The crystals of the original indolesulfamide changed into an oil on heating. During the reaction this oil crystallized. The crystals were filtered after cooling and washed on the filter with xylene. There was obtained 2.7 g of dark-brown substance which after recrystallization from water gave 1.25 g (55%) of 5-indolesulfamide. Colorless crystals, insoluble in benzene and gasoline, soluble in alcohol and dioxane. M. p. 203.5-204.5° (from aqueous alcohol).

Found %: C 49.37; H 4.45; S 16.34. $C_8H_8O_2N_2S$. Calculated %: C 48.97; H 4.11; S 16.34.

N,N-Dimethylamide of 5-indolesulfonic acid (XI). A solution of 1.2 g of the N,N-dimethylamide (VIII) in 250 ml of xylene and 2.4 g of chloranil was heated at the boil for 4 hours. After cooling, the product was washed in succession with alkali, water, dilute hydrochloric acid and water. The xylene was taken off in vacuo to leave 0.68 g (57%) of colorless crystals of N,N-dimethylamide of 5-indolesulfonic acid (XI) with m. p. 123-125° (from water and then from benzene).

Found %: N 11.88. $C_{10}H_{12}O_2N_2S$. Calculated %: N 12.49.

N-Methyl-N-phenylamide of 5-indolesulfonic acid (XII). A xylene solution of 1.12 g of N-methyl-N-phenylamide (IX) and 0.96 g of chloranil was heated at the boil for 4 hours and the product worked up as described for the preceding experiment. Removal of the xylene in vacuo left an oil to which a little heptane was added. The oil crystallized after a few hours to give 0.73 g (66%) of (XII). It slowly recrystallized from water in the form of colorless crystals with m. p. 102-103°.

Found %: C 62.80; H 5.04; S 11.11; N 9.82. $C_{15}H_{14}O_2N_2S$. Calculated %: C 62.90; H 4.93; S 11.19; N 9.78.

LITERATURE CITED

1. A. P. Terent'ev, M. N. Preobrazhenskaya, and G. M. Sorokina, Zhur. Obshch. Khim. 29, 2875 (1959).*
2. V. V. Feofilaktov and N. K. Semenova, Zhur. Obshch. Khim. 23, 644 (1953).*
3. U. S. Patent 1,866,956; Chem. Abs. 26, 4723 (1923).
4. French Patent 732,392; Chem. Abs. 27, 1010 (1933).
5. R. Giuliano and M. Stein, Ref. Zhur. Khim. (1958), p. 28976.
6. O. Süs and K. Möller, Lieb. Ann. 593, 91 (1955).
7. Synth. Org. Prep., Coll. Vol. I, 466 (1949).
8. N. I. Amiantov and V. A. Titkov, Anilinokrasoch. Prom. 2, 8-9 (1932).
9. M. Hayduck, Lieb. Ann. 172, 204 (1874).
10. R. Johnson and S. Smiles, J. Chem. Soc. 123, 2384 (1923).
11. R. Gnehm and E. Blumer, Lieb. Ann. 304, 87 (1898).
12. K. Saunders, Aromatic Diazo Compounds and Their Technical Utilization [Russian translation] (GONTI NKTP, 1938), p. 135.
13. A. P. Terent'ev and M. N. Preobrazhenskaya, Zhur. Obshch. Khim. 29, 317 (1959).*
14. A. P. Terent'ev, M. N. Preobrazhenskaya, A. S. Boblov, and G. M. Sorokina, Zhur. Obshch. Khim. 29, 2541 (1959).*
15. Ng. Buu-Hoi, B. Eckert, and R. Royer, Compt. rend. 233, 627 (1951).
16. O. A. Reutov, Theoretical Problems of Organic Chemistry [in Russian] (Izd. MGU, 1956), p. 363.
17. E. Royals, Advanced Organic Chemistry (1954), p. 509.
18. M. Kulka and R. Manske, Can. J. Chem. 30, 720 (1952).

* Original Russian pagination. See C. B. translation.

SUBSTITUTED ARYLAMIDES OF DITHIOCARBONIC ACIDS

I. SYNTHESIS OF ALKOXY-SUBSTITUTED N-PHENYLDITHIOOXAMIDES

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Dithiooxamide and its derivatives have been studied in recent years as analytical reagents [1], and their antibacterial [2] and insecticidal [3] properties have been examined. Some of them have proved to be good metal deactivators in petroleum products [4].

The only representatives of the series of substituted N-phenyldithiooxamides hitherto known were the phenyl, p-tolyl-, o-tolyl, 2,4-dimethylphenyl, and α- and β-naphthyl derivatives. Interest was therefore attached to the synthesis and examination of alkoxy-substituted derivatives which have not been mentioned at all in the literature.

Substituted N-phenyldithiooxamides can be obtained by two methods: Heating of substituted phenyloxamides with phosphorus pentasulfide in high-boiling organic solvents [5] and reduction of nitriles of the corresponding thiooxanilic acids by ammonium polysulfide [6].

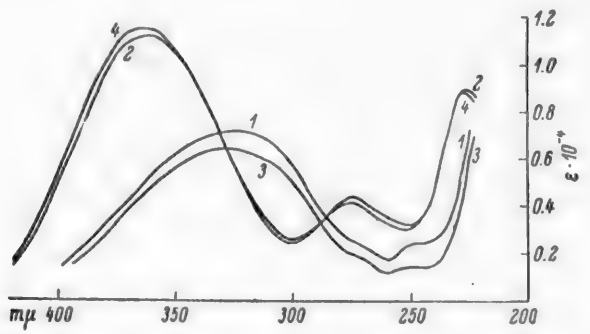


Fig. 1. Absorption spectra of nitriles of alkoxy-substituted thiooxanilic acids in the ultraviolet. 1) Nitrile of o-ethoxyphenylamide of thiooxalic acid; 2) nitrile of p-ethoxyphenylamide of thiooxalic acid; 3) nitrile of o-n-butoxyphenylamide of thiooxalic acid; 4) nitrile of p-n-butoxyphenylamide of thiooxalic acid.

The second was found the more convenient. The starting substances for preparation of substituted nitriles of thiooxanilic acid were the corresponding mustard oils. The latter were prepared from aromatic amines and thiophosgene in a medium of hydrochloric acid [1].

Nitriles of thiooxanilic acid are usually prepared by reaction of mustard oils in alcoholic solutions with an aqueous solution of potassium thiocyanate [6]. We prepared five nitriles by this method (Table 1, Nos. 1, 2, 4, 9 and 10). The remaining nitriles were prepared by reaction of the corresponding phenyl mustard oils with acetone cyanohydrin. In recent years the latter substance has been extensively used (as a source of hydrogen cyanide) in various addition and substitution reactions [8]. This last method leads to nitriles of thiooxanilic acid in good yields and in a fairly pure state. The great advantages of acetone cyanohydrin are the facility with which it can be measured out and its solubility in water and organic solvents. The synthesized alkoxylated nitriles of thiooxanilic acid are listed in Table 1.

We see from Table 1 that the nitriles are obtained in good yields. They form yellow crystals, readily soluble in caustic alkali and in alcohol and other organic solvents. They were purified by crystallization from alcohol.

Absorption curves of nitriles of o- and p-ethoxy- and n-butoxyphenylamidothiooxalic acid in 10^{-4} M concentration in alcohol are plotted in Fig. 1.

We see from Fig. 1 that the absorption maximum of para-substituted derivatives is located at longer wavelengths than the principal absorption maximum of the corresponding ortho-substituted compounds.

Alkoxyphenyldithiooxamides were prepared by saturation of an alcoholic solution of the corresponding nitrile with gaseous ammonia and then with hydrogen sulfide. Completion of saturation with hydrogen sulfide was followed by separation of orange-red crystals or oil. The latter crystallized after purification (from alcohol).

Alkoxyphenyldithiooxamides can be obtained without isolation of the nitriles of thiooxanilic acid. For this purpose the alcoholic solutions of the nitriles, obtained by reaction of mustard oils with acetone cyanohydrin in an alkaline medium, are saturated with hydrogen sulfide, and the resulting product is purified in the usual way. Table 2 contains the names of the alkoxyphenyldithiooxamides that we synthesized, together with their melting points, yields and analyses.

Figure 2 contains absorption curves of o- and p-ethoxy- and n-butoxyphenyldithiooxamides in 10^{-4} M concentration in alcohol.

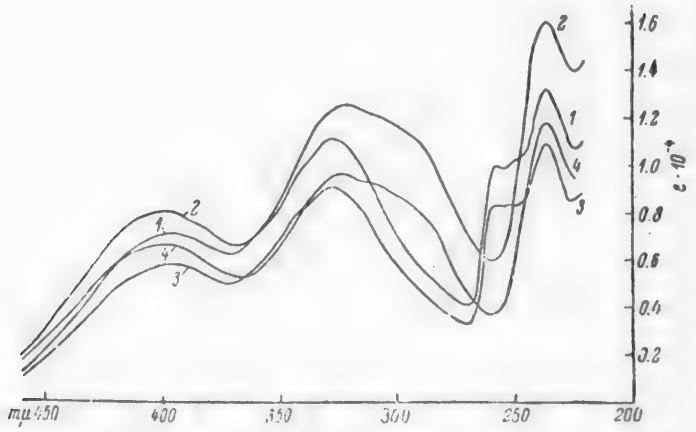
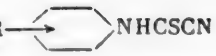


Fig. 2. Ultraviolet absorption spectra of alkoxy-substituted phenyldithiooxamide; 1) o-ethoxyphenyldithiooxamide; 2) p-ethoxyphenyldithiooxamide; 3) o-n-butoxyphenyldithiooxamide; 4) p-n-butoxyphenyldithiooxamide.

The absorption curves of ortho-substituted compounds are seen to differ from those of para-substituted compounds by the presence of a plateau in the 250-270 mμ region.

TABLE 1

Alkoxylated Nitriles of Thiooxanilic Acid with the General Formula 

Prep. No.	R	Yield (in %)	Melting point	Color of crystals	Empirical formula	% N		% S	
						found	calc.	found	calc.
1	o-Methoxy	79	108°	Brown	$C_9H_8ON_2S$	—	—	16.54, 16.55	16.66
2	p-Methoxy	96	118—119	Yellow	$C_9H_8ON_2S$	—	—	17.00, 16.88	16.66
3	o-Ethoxy	65	70— 72	Yellow	$C_{10}H_{10}ON_2S$	—	—	15.25, 15.37	15.53
4	p-Ethoxy	65	111—112	Yellow	$C_{10}H_{10}ON_2S$	—	—	15.72, 15.55	15.53
5	o-n-Propoxy	91	59— 60	Yellow	$C_{11}H_{12}ON_2S$	12.65, 12.80	12.72	—	—
6	p-n-Propoxy	96	103—104	Yellow	$C_{11}H_{12}ON_2S$	—	—	14.48, 14.32	14.54
7	o-Isopropoxy	93	54— 55	Light brown	$C_{11}H_{12}ON_2S$	12.11, 11.98	12.72	—	—
8	p-Isopropoxy	91	58— 60	Yellow-orange	$C_{11}H_{12}ON_2S$	12.62, 12.69	12.72	—	—
9	o-n-Butoxy	29*	87— 88	Yellow	$C_{12}H_{14}ON_2S$	—	—	13.52, 13.52	13.67
10	p-n-Butoxy	98	85— 86	Yellow	$C_{12}H_{14}ON_2S$	—	—	13.56, 13.64	13.67
11	o-Isobutoxy	95	92	Yellow	$C_{12}H_{14}ON_2S$	—	—	13.48, 13.57	13.67
12	o-Isoamyloxy	98	98	Orange	$C_{13}H_{16}ON_2S$	—	—	13.29, 13.06	12.90

* Low yield of nitrile due to isolation after solution of the mustard oil without leaving the reaction mixture until the next day.

TABLE 2

Alkoxy Derivatives of Phenyldithiooxamide with the General Formula R–C$_6$H$_4$–NHCSCSNH$_2$

Prep. No.	R	Yield (in %)	Melting point	Color of crystals	Empirical formula	% N		% S	
						found	calc.	found	calc.
1	o-Methoxy	26	123—124°	Orange	$C_9H_{10}ON_2S_2$	12.39, 12.22	12.38	—	—
2	p-Methoxy	45	142—143	Red-orange	$C_9H_{10}ON_2S_2$	11.91, 12.01	12.38	—	—
3	o-Ethoxy	38	109	Red	$C_{10}H_{12}ON_2S_2$	11.46, 11.41	11.66	26.44, 26.56	26.66
4	p-Ethoxy	57	112—113	Orange-red	$C_{10}H_{12}ON_2S_2$	—	—	26.65, 26.72	26.66
5	o-n-Propoxy	27	130—131	Red	$C_{11}H_{14}ON_2S_2$	—	—	25.13, 25.22	25.19
6	p-n-Propoxy	30	85	Red	$C_{11}H_{14}ON_2S_2$	11.33, 11.42	11.02	—	—
7	o-Isopropoxy	17	110—111	Red	$C_{11}H_{14}ON_2S_2$	—	—	25.05, 24.87	25.19
8	p-Isopropoxy	43	65	Red	$C_{11}H_{14}ON_2S_2$	11.16, 11.10	11.02	—	—
9	o-n-Butoxy	37	94	Red	$C_{12}H_{16}ON_2S_2$	10.19, 9.99	10.59	—	—
10	p-n-Butoxy	31	85— 86	Red	$C_{12}H_{16}ON_2S_2$	10.25, 10.27	10.39	—	—
11	o-Isobutoxy	22	100—101	Red	$C_{12}H_{16}ON_2S_2$	10.20, 10.15	10.39	—	—
12	o-Isoamyloxy	32	94— 95	Red	$C_{13}H_{18}ON_2S_2$	9.85, 9.82	9.92	—	—

EXPERIMENTAL

Nitrile of p-n-butoxyphenylamide of thiooxalic acid. To a solution of 9.3 g of p-n-butoxyphenyl mustard oil in 50 ml of alcohol was added 2.8 g of sodium cyanide in 15 ml of water. The mixture was stirred for 2-3 hours and left until the next day. The solution was then filtered, diluted with water and acidified with hydrochloric acid. The resulting yellow precipitate was filtered off, washed on the funnel with water and dried. Yield 10.3 g.

Nitrile of o-ethoxyphenylamide of thiooxalic acid. To a solution of 4 g of o-ethoxyphenyl mustard oil in 10 ml of alcohol was added 3 ml of acetone cyanohydrin and 1 g of sodium hydroxide diluted with 10 ml of water. The mixture was periodically shaken until the mustard oil had completely dissolved after separation on addition of the aqueous alkali. During this operation the color gradually changed to light-brown. The mixture was left until the next day. The solution was then filtered, diluted with water and acidified with hydrochloric acid. Dilution with water caused turbidity; acidification brought down a yellow precipitate which was filtered off, washed with water and dried. Nitriles listed in Table 1 as Nos. 3, 5, 6, 7, 8, 11, and 12 were prepared under similar conditions.

o-Isobutoxyphenyldithiooxamide. The nitrile of o-isobutoxyphenylamide of thiooxalic acid (3.5 g) was dissolved in 25 ml of dilute alcohol (20 ml of alcohol mixed with 5 ml of water) and gaseous ammonia was passed through and then a stream of hydrogen sulfide. Saturation with hydrogen sulfide was followed by separation of an oil. The reaction mixture was diluted with a little water and acidified with hydrochloric acid. The resulting crystals (permeated with oil) were filtered off, washed with water and recrystallized from alcohol. Yield 0.9 g. Bright-red crystals. With exception of No. 12, the alkoxy derivatives listed in Table 2 were prepared in similar fashion.

o-Isoamyloxyphenyldithiooxamide. o-Isoamyloxyphenyl mustard oil (0.7 g) was dissolved in 5 ml of alcohol and to the solution were added 0.5 ml of acetone cyanohydrin and 0.2 g of sodium hydroxide in 5 ml of water. The mustard oil separated when the alkali solution was added but gradually redissolved after periodic shaking for 3-4 hours. The mixture was left until the next day. The mixture was then filtered and the filtrate saturated with hydrogen sulfide. During passage of the hydrogen sulfide the color changed from light-brown to yellow-red and an oily substance came out. More complete separation of the product was effected by addition of water. The upper aqueous alcoholic solution was poured off and the oil extracted with ether. The extract was dried with calcined sodium sulfate and filtered; the solvent was removed in vacuo. Cooling of the residue in iced water caused it to crystallize in the form of red needles which were filtered from oil, washed with a little alcohol and dried. Yield 0.25 g.

SUMMARY

1. Reaction of alkoxy-substituted phenyl mustard oils with acetone cyanohydrin or with sodium cyanide in an alcoholic medium gave twelve new alkoxy-substituted nitriles of thiooxanilic acid.

2. Saturation of alcoholic solutions of the nitriles with gaseous ammonia and then with hydrogen sulfide gave twelve alkoxy-substituted N-phenyldithiooxamides.

3. The absorption spectra of some of the synthesized compounds were plotted.

LITERATURE CITED

1. P. Ray, Z. Anal. Chem. 79, 94 (1929); F. Feigl and H. Kapultzas, Mikrochemie 8, 239 (1930); S. A. Voznesenskii, Inner-Complex Compounds and Their Value in Analytical Chemistry [in Russian] (GONTI, 1938), p. 79; L. M. Kul'berg, Syntheses of Organic Reagents for Inorganic Analysis [in Russian] (Moscow-Leningrad, 1947), p. 119.
2. K. Liebermeister, Z. Naturforsch. 56, 79 (1950); Chem. Abs. 7986 i (1950).
3. U. S. Patent 2,525,075 (1950); Chem. Abs. 2499d (1951).
4. U. S. Patent 2,484,257 (1949); Chem. Abs. 5575 c (1950).

5. A. Reissert, Ber. 37, 3716 (1904).
6. A. Reissert and K. Bruggenann, Ber. 57, 982 (1924).
7. D. McKee and R. W. Rost, J. Am. Chem. Soc. 68, 2506 (1946).
8. I. N. Nazarov, A. V. Semenovskii, and A. V. Kamernitskii, Izvest. Akad. Nauk SSSR (1957), p. 976; I. N. Nazarov and S. I. Zav'yalov, Zhur. Obshch. Khim. 24, 466 (1954);* I. N. Nazarov, A. A. Akhrem, and A. V. Kamernitskii, Zhur. Obshch. Khim. 25, 1345 (1955).*

*Original Russian pagination. See C. B. translation.

REACTIONS OF HALOMETAL ALCOHOLATES

VII. INTERACTION OF HALOMAGNESIUM CARBINOLATES OF TERTIARY ALCOHOLS WITH ESTERS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1227-1230, April, 1960
Original article submitted March 2, 1959

Halomagnesium alcoholates of alcohols are known to be the end products of the reaction between organomagnesium compounds and aldehydes, ketones, esters and chlorides of carboxylic acids. In some cases, however, these reactions lead to formation of unsaturated compounds. Splitting-off of part of the water is most frequently observed in the synthesis of tertiary alcohols and less often in the synthesis of secondary and primary alcohols. Examination of the conditions of all these reactions shows that unsaturated compounds are formed most frequently when alkylmagnesium iodides or arylmagnesium iodides are taken as the organomagnesium compounds. The iodo compounds are unstable and liberate iodine which is known to be a dehydrating agent for tertiary alcohols [1-3].

Conversion of halomagnesium alcoholates into unsaturated hydrocarbons goes even better in presence of one excess mole of the alkylmagnesium iodide and with heating at 100° for 6 hours [4]. Unsaturated compounds are formed instead of alcohols if the reaction products, without their decomposition with water and acids, are directly distilled in vacuo [5]. Unsaturated compounds containing phenyl radicals are easily formed instead of secondary and tertiary alcohols if the para position of this radical contains a hydroxy [6], alkoxy [7] or dialkylamino group [8-10]. Finally, dehydration of alcohols with formation of unsaturated hydrocarbons is also observed in some reactions of organomagnesium compounds with acid chlorides [11-12].

Judging by all these examples, dehydration occurs only under special conditions. It appears that halomagnesium alcoholates (even tertiary) are relatively stable compounds; formation of unsaturated hydrocarbons instead of alcohols must be due to an excess of one component which reacts with the alcoholate as formed and lowers its stability. For example, an excess of ethyl formate in its reaction with arylmagnesium halides completely changes the character of the end product (diarylmethyl halide is formed instead of diarylcarbinol). The reaction course is also altered by esters of such acids as oxalic, malonic, succinic and sulfuric [13].

The fact that excess of one component or deliberate introduction of a third component can change the direction of the organomagnesium reaction was exploited by us for regulation of the reaction of ketones with organomagnesium compounds with the objective of obtaining unsaturated hydrocarbons in place of alcohols. As the third component we selected ethyl formate (also ethyl oxalate). The resulting unsaturated hydrocarbons were slightly contaminated with starting substances that masked the reaction course.

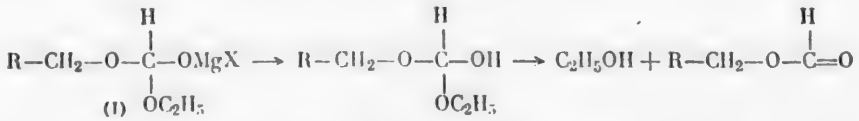
Studies were also made of the reactions of halomagnesium carbinolates, prepared from pure carbinols and ethyl formate, with the aim of obtaining an accurate picture of the reaction and of the nature of the resulting products.

The experimental results (see table) show that bromomagnesium alcoholates of tertiary aliphatic and fatty-aromatic alcohols are converted in presence of equimolar amounts of ethyl formate into unsaturated hydrocarbons and in part into bromides. However, in presence of the same ester, alcoholates of tertiary alcohols containing two

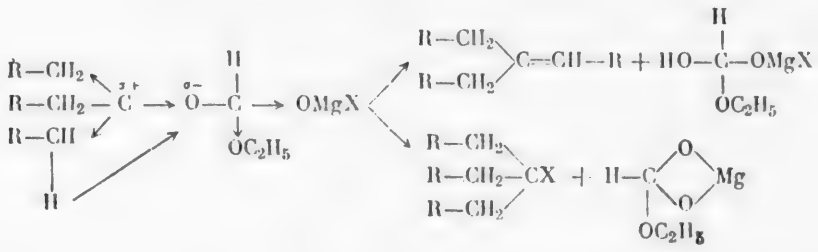
Unsaturated Hydrocarbons

Prep. No.	Reaction components (1 : 1)	Composition of reaction product (in %)		Name of unsaturated hydrocarbon	Constants of unsaturated hydrocarbon experimental data			MR_D		Literature
		Unsat. hydrocarbon	Bromide		boiling point (pressure in mm)	$n^{20}D$	d^{20}_4	found	calc.	
1	MgBr-Dimethyl-n-butylcarbinolate and ethyl formate	69	31	2-Methylhexene-2	94-95°	–	–	–	–	[14]
2	MgBr-Dimethylisobutylcarbinolate and ethyl formate	83	17	2,4-Dimethylpentene-2	83-84°	–	–	–	–	[15]
3	MgBr-Dimethylphenylcarbinolate and ethyl formate	80	20	α-Methylstyrene	160-161	1.5325	0.9055	40.42	39.69	[16]
4	MgBr-Diethylphenylcarbinolate and ethyl formate	90	10	β-Methyl-α-ethylstyrene	197-198	1.5256 (at 16°)	0.9167 (at 16°)	48.88	48.93	[17]
5	MgBr-Di-n-propylphenylcarbinolate and ethyl formate	81	19	β-Ethyl-α-n-propylstyrene	118-120 (25)	1.5190 (at 17.5°)	0.9109 (at 17.5°)	57.98	58.18	[18]
6	MgBr-Di-n-butylphenylcarbinolate and ethyl formate	82	18	β-n-Propyl-α-n-butylstyrene	118-120 (10)	1.5222 (at 17°)	0.9200 (at 17°)	67.11	67.43	[19]
7	MgBr-Diisobutylphenylcarbinolate and ethyl formate	80	20	β-Isopropyl-α-isobutylstyrene	131-133 (28)	1.5168 (at 18°)	0.9059 (at 18°)	67.45	67.43	–
8	MgBr-Dimethyl-o-tolylcarbinolate and ethyl formate	95	5	α-p-Dimethylstyrene	72-74 (10)	1.5286 (at 16°)	0.9100 (at 16°)	44.72	44.41	[20]
9	MgBr-Dimethyl-p-tolylcarbinolate and ethyl formate	97	3	α-p-Dimethylstyrene	80-82 (10)	1.5140	0.9257	43.95	44.41	[20]
10	MgBr-Dimethyl-3,4-dimethylphenylcarbinolate and ethyl formate	83	17	α-3,4-Trimethylstyrene	95-97 (15)	1.5320	0.9330	49.63	48.94	–
11	MgBr-Dimethyl-2,5-dimethylphenylcarbinolate and ethyl formate	73	27	α-2,5-Trimethylstyrene	68 (7)	1.5210	0.9067	49.05	48.94	–
12	MgBr-Methyldiphenylcarbinolate and ethyl formate	100	–	α,α-Diphenylethylene	133-134 (11)	1.6040	1.0250	60.40	59.19	[21]
13	MgBr-Methylphenyl-o-tolylcarbinolate and ethyl formate	100	–	α-Phenyl-α-o-tolylethylene	140-142 (10)	1.5808	1.0160	64.10	63.79	[22]
14	MgBr-Methylphenyl-p-tolylcarbinolate and ethyl formate	100	–	α-Phenyl-α-p-tolylethylene	146-148 (8)	1.5775	1.0110	63.63	63.78	[23]
15	MgBr-Dimethylmesitylcarbinolate and ethyl formate	100	–	α-Methyl-α-mesitylethylene	204-206	–	–	–	–	[24]

aryl radicals are smoothly converted into unsaturated hydrocarbons [25]. Reaction of halomagnesium alcoholates of primary alcohols with ethyl formate leads to formation of a stable addition compound (I) which is converted by dilute acid into an unstable ester of orthoformic acid whose stabilization is accompanied by detachment of the more electronegative ethoxyl group with formation of an ester of formic acid.



Halomagnesium alcoholates of tertiary alcohols form with formic acid esters a less stable compound (type I) which stabilizes with formation mainly of unsaturated hydrocarbons (main reaction) and of bromides in a secondary reaction. The latter becomes the main reaction when halomagnesium diarylcarbinolates are reacted [13, 25].



The compound (type I) formed by secondary alcohols is intermediate in stability between the analogous compounds formed by primary and tertiary alcohols. Products of stabilization of this compound are esters, unsaturated hydrocarbons and bromides.

Dehydration proceeds with the greatest facility on reaction of esters of formic acid with halomagnesium alcoholates of tertiary alcohols containing aryl radicals. This is explained by the development of a larger fractional negative charge at the oxygen atom nearest to the radicals in association with the greater electronegativity of the phenyl radical. Dehydration is also thereby facilitated when use is made of esters of stronger acids (e.g., on replacement of ethyl formate by diethyl oxalate).

EXPERIMENTAL

Reaction between bromomagnesium carbinolates of tertiary alcohols and ethyl formate. To a solution of tertiary alcohol in three times the volume of absolute ether was added an ethereal solution (three volumes of ether) of ethylmagnesium bromide freed of excess of magnesium (the ethylmagnesium bromide content of the ethereal solution was determined by titration with hydrochloric acid solution). Into the ethereal solution of bromomagnesium carbinolate was stirred an equimolar amount of ethyl formate dissolved in the same volume of absolute ether. The reaction mixture was heated for 2 hours and then decomposed with water and 10% acetic acid. The ether layer was washed with 10% sodium bicarbonate solution and then with water until neutral. After the ethereal solution had been dried with calcined sodium sulfate, the solvent was driven off and the product investigated. A bromine determination gave the amount of bromide and a hydroxyl group determination the amount of carbinol. The product was then distilled in vacuo and the unsaturated hydrocarbon fraction was purified from bromide by treatment with alcoholic silver nitrate before redistillation.

Dimethyl-(3,4-dimethylphenyl)-carbinol was synthesized from 3,4-dimethylphenylmagnesium bromide and acetone under the usual conditions. Yield 65%. Not described in the literature.

B. p. 116-118° (7 mm), d^{20}_4 1.0040, $n^{20}D$ 1.5268, MR_D 50.17; calc. 50.93.

Found %: C 80.31; H 9.65. $C_{11}H_{16}O$. Calculated %: C 80.48; H 9.76.

Dimethyl-(2,5-dimethylphenyl)-carbinol. Synthesized from 2,5-dimethylphenylmagnesium bromide and acetone. Yield 60%. Not described in the literature.

B. p. 145-146° (27 mm), m. p. 39° (from ligroine).

Found %: C 80.52; H 9.95. $C_{11}H_{16}O$. Calculated %: C 80.48; H 9.76.

Methylphenyl-o-tolylcarbinol. Synthesized from o-tolylmagnesium bromide and acetophenone. Yield 40%. Not described in the literature.

B. p. 151-153° (10 mm), d^{18}_4 1.0447, $n^{18}D$ 1.5540, MR_D 65.09; calc. 65.80.

Found %: C 84.71; H 7.55. $C_{15}H_{16}O$. Calculated %: C 84.90; H 7.54.

Diisobutylphenylcarbinol. Prepared by reaction of isobutylmagnesium bromide with methyl benzoate. Yield 75%. Not described in the literature.

B. p. 118-120° (16 mm), d^{16}_4 0.9312, $n^{16}D$ 1.4990, MR_D 69.42; calc. 69.41.

Found %: C 81.58; H 10.89; OH 7.40. $C_{15}H_{24}O$. Calculated %: C 81.76; H 10.98; OH 7.70.

SUMMARY

1. The reaction between bromomagnesium carbinolates of tertiary alcohols and ethyl formate was studied. It was established that the main products of the reaction are unsaturated hydrocarbons with bromides as secondary products.

2. The results of the investigation can be utilized, as confirmed experimentally, for regulation of organomagnesium reactions with the aim of obtaining unsaturated hydrocarbons instead of tertiary alcohols.

3. The mechanism of reaction of halomagnesium alcoholates of tertiary alcohols with esters was studied.

4. Some new fatty-aromatic tertiary alcohols and unsaturated hydrocarbons were synthesized and described.

LITERATURE CITED

1. V. Grignard, Compt. rend. 130, 1322 (1900).
2. B. Brooks and J. Humphrey, Zbl. II, 522 (1918).
3. A. Klages and Santter, Ber. 37, 649 (1901).
4. A. Klages, Ber. 35, 2640 (1902).
5. F. Sachs and L. Sachs, Ber. 38, 511 (1905).
6. A. Behal and M. Tiffeneau, Zbl. I, 1624 (1908).
7. G. Busignies, Zbl. II, 1471 (1910).
8. M. Freund and F. Mayer, Ber. 39, 1117 (1906).
9. P. Lemoult, Zbl. II, 2041 (1913).
10. H. Fecht, Ber. 40, 3893 (1907).
11. Tissier and V. Grignard, Zbl. I, 1357 (1901).
12. V. Grignard, Zbl. I, 1077 (1903).
13. I. I. Lapkin and O. M. Lapkina, Zhur. Obshch. Khim. 25, 298 (1955).*
14. F. J. Soday and C. E. Boord, Zbl. II, 2255 (1933).
15. S. P. Mulliken, R. L. Wakeman, and H. F. Gerry, Zbl. I, 1847 (1936).
16. Beilstein 5, 484 (4th edition).
17. Beilstein 5, 498 (4th edition).

* Original Russian pagination. See C. B. translation.

18. A. S. Broun, M. G. Voronkov, and P. A. Shlyakhter, Byull. Leningrad. Gosudarst. Univ. 18, 11 (1947).
19. A. D. Petrov, A. P. Baidanov, N. I. Zakotin, and P. I. Suntsev, Zhur. Obshch. Khim. 9, 509 (1939).
20. Beilstein 5, 490 (4th edition).
21. Beilstein 5, 639 (4th edition).
22. E. Bergman and A. Bondi, Zbl. I, 2095 (1933).
23. Beilstein 5, 645 (4th edition).
24. M. S. Newman and N. C. Deno, J. Am. Chem. Soc. 73, 3644 (1951).
25. I. I. Lapkin, O. M. Lapkina, and M. N. Rybakova, Zhur. Obshch. Khim. 28, 391 (1958).*

* Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF THIOINDIGOID DYES

IV. MONONITRO-SUBSTITUTED THIOINDIGOES

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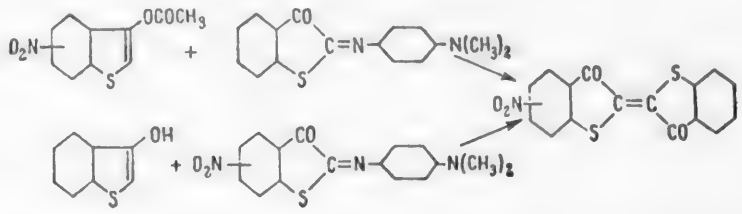
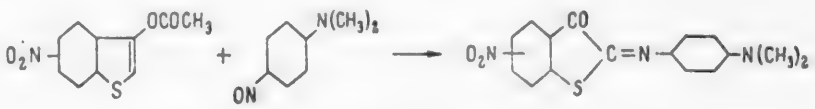
In connection with our understanding of the rules governing the color of thioindigoid dyes, it was of interest to compare the colors of monosubstituted thioindigoes with those of the corresponding disubstituted and the unsubstituted dyes. Monochloro-, monomethyl- and monoethoxythioindigo have been described [1] but the colors were not compared.

We synthesized 5- and 6-mononitrothioindigo and measured the absorption spectra of their solutions in benzene. The dyes were prepared by condensation of the corresponding nitroacetoxythionaphthenes [2] with thionaphthenequinone-2-(p-dimethylamino)anil in acetic acid in presence of piperidine; they were also prepared by condensation under the same conditions of 3-hydroxythionaphthene with the corresponding nitrothionaphthenequinone-2-(p-dimethylamino)anils.



Nitrothionaphthenequinone-2-(p-dimethylamino)anils are formed by interaction of nitroacetoxythionaphthenes and p-nitrosodimethylaniline in aqueous sodium carbonate.



The nitroacetoxythionaphthenes entering into reaction with thionaphthenequinone-2-(p-dimethylamino)anil and with p-nitrosodimethylaniline manifest the same reactivity as 3-hydroxythionaphthene and its substituted derivatives.

The absorption maxima of solutions of mononitro-substituted thioindigoes in benzene are presented in the table.

The shift of the absorption maximum of mononitrothioindigo in relation to the unsubstituted dye ($\Delta\lambda$) is equal to the shift of the absorption maximum of each nitro group in the corresponding dinitro derivative $\frac{\Delta\lambda}{2}$.

We previously reported the absorption maxima of dinitro derivatives of thioindigo [2].

Prep. No.	Name of dye	λ_{max}	$\varepsilon_{max} \cdot 10^{-4}$	$\Delta\lambda$	$\frac{\Delta\lambda'}{2}$	$\Delta\lambda - \frac{\Delta\lambda'}{2}$
1	5-Nitrothioindigo	540	1.6	−5	−16	+11
2	6-Nitrothioindigo	561	1.8	+16	+11	+5

Unlike the unsymmetrical cyanine dyes, whose absorption maxima are shifted in the direction of the short-wave region relative to the arithmetic mean of the absorption maxima of the corresponding symmetrical dyes [3, 4], the color of mononitro derivatives of thioindigo is deeper than it would be if the nitro group in mononitrothioindigo had the same influence on color as each nitro group in the corresponding dinitro dyes.

EXPERIMENTAL

5-Nitrothionaphthenequinone-2-(p-dimethylamino)anil. To a solution of 5 g of anhydrous sodium carbonate in 400 ml of water were added 6.0 g of finely pulverized 5-nitro-3-acetoxythionaphthene and 4.0 g of p-nitrosodimethylaniline. The mixture was heated to 70° in an hour with stirring, and stirred at this temperature for 3 hours. The product was filtered without cooling and thoroughly washed with hot water. Yield 7.15 g (86.5%). Crystallization from chlorobenzene gave dark crystals with a bronzy luster; m. p. 265-266° (with decomp.).

Found %: N 12.75, 12.53; S 9.75, 9.94. $C_{16}H_{13}O_3N_3S$. Calculated %: N 12.83; S 9.80.

6-Nitrothionaphthenequinone-2-(p-dimethylamino)anil. To a solution of 5 g of anhydrous sodium carbonate in 400 ml of water were added 5.0 g of well-pulverized 6-nitro-3-acetoxythionaphthene and 3.6 g of p-nitrosodimethylaniline. The mixture was heated to 80° with stirring and stirred for 3 hours. The reaction product was filtered and washed with hot water. Yield 5.6 g (81%). Nearly black crystals were obtained by crystallization from chlorobenzene; m. p. 258-259° (decomp.).

Found %: N 12.55, 12.50; S 10.09, 10.13. $C_{16}H_{13}O_3N_3S$. Calculated %: N 12.83; S 9.80.

5-Nitrothioindigo. A mixture of 0.38 g of 3-hydroxythionaphthene, 0.82 g of 5-nitrothionaphthene-2-(p-dimethylamino)anil, 15 ml of acetic acid and 0.25 ml of piperidine was refluxed for 2 hours. After cooling, the dye was filtered off and washed with hot alcohol. Fine, red crystals, yield 0.79 g (93%). Crystallization from nitrobenzene gave dark-red crystals with m. p. 380-385° (decomp.).

Found %: N 4.35, 4.32; S 18.73, 18.92. $C_{16}H_7O_4NS_2$. Calculated %: N 4.10; S 18.79.

A mixture of 1.2 g of 5-nitro-3-acetoxythionaphthene, 1.4 g of thionaphthenequinone-2-(p-dimethylamino)anil, 25 ml of acetic acid and 0.5 ml of piperidine was boiled for 2 hours. The product was worked up as above. Yield of dye 1.35 g (79.5%).

6-Nitrothioindigo. By the same procedure as above, 0.38 g of 3-hydroxythionaphthene and 0.82 g of 6-nitrothionaphthenequinone-2-(p-dimethylamino)anil gave 0.78 g (91.5%) of dye in the form of dark-red powder. Crystallization from nitrobenzene gave dark-red crystals with m. p. 355-360° (decomp.).

Found %: N 4.30, 4.34; S 18.30, 18.45. $C_{16}H_7O_4NS_2$. Calculated %: N 4.10; S 18.79.

From 1.2 g of 6-nitro-3-acetoxythionaphthene and 1.4 g of thionaphthenequinone-2-(p-dimethylamino)anil was obtained (same procedure as for 5-nitrothioindigo) 1.35 g (79.5%) of 6-nitrothioindigo.

SUMMARY

1. 5- and 6-Mononitrothioindigo were synthesized and the absorption spectra of their solutions in benzene were measured.

2. The color of mononitrothioindigoes was compared with that of the corresponding dinitro derivatives and unsubstituted thioindigo.

LITERATURE CITED

1. C. . E. Dalgliesh and F. G. Mann, J. Chem. Soc. (1945), p. 903.
2. N. S. Dokunikhin and Yu. E. Gerasimenko, Zhur. Obshch. Khim. 30, 635 (1960). *
3. A. I. Kiprianov, Doklady Akad. Nauk USSR 12, 3 (1940).
4. L. G. S. Brooker and R. H. Sprague, J. Am. Chem. Soc. 63, 3203 (1941).

* Original Russian pagination. See C. B. translation.

AMIDATION OF SOME COMPOUNDS OF TRIVALENT PHOSPHORUS

K. A. Petrov and O. S. Urbanskaya

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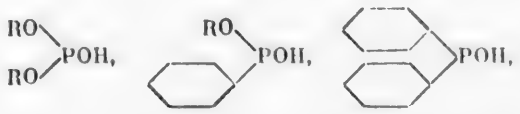
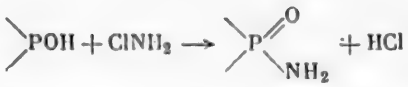
Acid phosphites, like neutral phosphites, are known to enter into the Arbuzov reaction with various compounds such as alkyl hypochlorites [1], sulfenyl chlorides [2] and chloroamines [3], to give, respectively, trialkyl phosphates, O-dialkyl-S-alkyl phosphates and dialkylamides of dialkylphosphoric acid. These reactions, like numerous reactions of neutral esters of phosphorous and phosphinous acids [4], are governed by the ability of trivalent phosphorus to add on to various substances with formation of intermediate, usually unstable, products with onium structure which are transformed into diverse compounds of pentavalent phosphorus.

The aim of the present work was to study reactions of chloramide with compounds of the type of

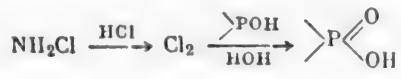


that could lead to a new method of synthesis of amides of phosphoric and phosphinic acids. Direct amidation of compounds of trivalent phosphorus can prove useful for preparation of substances containing a phosphamido group which (like the sulfamido group) can endow compounds with pharmacological properties.

Compounds brought into reaction with chloramide were di-n-butyl, diisoamyl and di-n-hexyl phosphites, monoisoamylphenyl phosphonite, and diphenylphosphinous acid. It was found that best results are obtained if an aqueous solution of chloramide is stirred into the cooled compounds of trivalent phosphorus (reaction mixture at a temperature of − 5 to + 30°). Under these conditions the reaction goes with formation mainly of phosphamide.



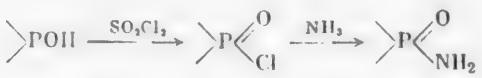
The reverse order of mixing of reactions or a higher reaction temperature leads to formation in appreciable amounts, and sometimes as the main product, of acid phosphates, phosphonates and phosphinic acids.



Onium products of addition of chloramide to trivalent phosphorus could not be detected under the above conditions of synthesis due to the ease of their breakdown with water [3].

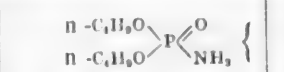
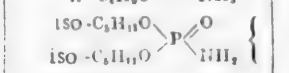
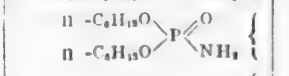
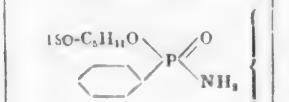
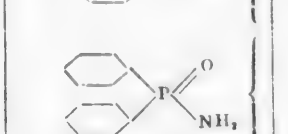
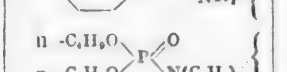
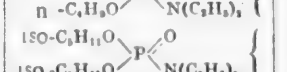
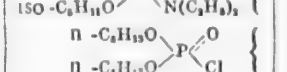
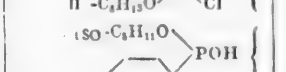
Compounds prepared by this route were di-n-butyl, diisoamyl and di-n-hexyl amidophosphates, pentoxyamidophenyl phosphonate and amidodiphenyl phosphonate. The first three substances are liquids that distill in vacuo. Di-n-hexyl amidophosphate partly decomposes during distillation in vacuo (0.23 mm), and analysis

shows that it becomes less pure than before distillation. The last two substances form colorless crystals. Pentoxyamidophenyl phosphonate is soluble in all common organic solvents except heptane; amidodiphenyl phosphonate is readily soluble in polar solvents and poorly soluble in nonpolar solvents. All the above compounds, except diisoamyl amidophosphate, were also prepared by the usual method.



In this case, however, the amide of pentoxyphenylphosphinic acid is obtained in a less pure form, and the amide of diphenylphosphinic acid in lower yield than by the method of direct amidation. At the same time it should be noted that direct amidation cannot always be recommended for the synthesis of phosphamides. For example, N-diethylamidodibutyl- and N-diethylamidodiamylphosphates are obtained in admixture with difficultly separable impurities and in lower yields than by the method of replacement of the chlorine in the respective chlorophosphates by the diethylamido group.

Structural formulas and yields of substances not described in the literature are set forth in the table.

Prep. No	Formula of compound prepared	Reactants	Yield (in %)
(I)		$(C_4H_9O)_2POH$ NH_3Cl	62
(II)		$(C_5H_{11}O)_2POH$ NH_3Cl	70
(III)		$(C_6H_{13}O)_2POH$ NH_3Cl	82 * 56
(IV)		$C_6H_5P(OC_5H_{11})OH$ NH_3Cl $C_6H_5P(OC_5H_{11})OH$ SO_2Cl_2 NH_3	65 60
(V)		$(C_6H_5)_2POH$ NH_3Cl $(C_6H_5)_2POH$ SO_2Cl_2 NH_3	47 ** 32
(VI)		$(C_4H_9O)_2P(O)Cl$ $NH(C_2H_5)_2$	83
(VII)		$(C_5H_{11}O)_2P(O)Cl$ $NH(C_2H_5)_2$	74
(VIII)		$(C_6H_{13}O)_2POH$ SO_2Cl_2	79
(IX)		$C_6H_5PCl_2$ $C_5H_{11}OH$	64

* Before distillation.

** Diphenylphosphinic acid was obtained at the same time in 35% yield.

EXPERIMENTAL*

1. Synthesis of di-n-butylamidophosphate (I). a) To 12 g of di-n-butyl phosphite with stirring and cooling was added a freshly prepared solution of 3.8 g of chloramide** in the course of an hour in 15-20 ml portions. The temperature of the reaction mixture rose after addition of the first portion (from − 5 to + 25°) and hardly changed subsequently. The reaction mass was then stirred for 2 hours without cooling, and the temperature rose to 10° above room temperature. The product was extracted with ether. The ethereal solution was washed with a little 10% NaOH and then with water until neutral. It was dried with $MgSO_4$ and fractionated to give 8 g of dibutyl amidophosphate.

B. p. 172-174° (8 mm), 123-126° (0.2 mm), $n^{20}D$ 1.4353, d^{20}_4 1.0363.

Found %: N 6.68. $C_8H_{20}O_3NP$. Calculated %: N 6.69.

Acidification of the aqueous solution followed by ether extraction yielded 1.7 g of dibutyl phosphate.

b) To an aqueous solution of 2.6 g of chloramide was added 8 g of dibutyl phosphite in the course of 0.5 hour under the conditions of Expt. 1a. There was obtained 1.2 g (14%) of dibutyl amidophosphate and 3.9 g (45%) of dibutylphosphoric acid.

c) An aqueous solution of 7.4 g of chloramide was added to 22.5 g of dibutyl phosphite under the conditions of 1a with the sole difference that after addition of the chloramide the temperature of the reaction mixture rose spontaneously to 40°. There were obtained 3.6 g (17%) of dibutyl amidophosphate and 12 g (49%) of dibutylphosphoric acid.

d) Dibutyl chlorophosphate (16 g) was dissolved in two volumes of ether and saturated (cooling) with dry ammonia. The ethereal solution was freed of ammonium chloride, washed with water and dried. The dibutyl amidophosphate distilled over at 182-185° (13 mm) in the amount of 7.2 g (49.3%).

2. Synthesis of diisoamyl amidophosphate (II). Reaction was effected as in Expt. 1a but was accompanied by less liberation of heat. From 14.1 g of diisoamyl phosphite and 4 g of chloramide, dissolved in 86 ml of water, was obtained 14.1 g of diisoamyl amidophosphate.

B. p. 142-143° (0.2 mm), $n^{20}D$ 1.4392, d^{20}_4 1.0061.

Found %: N 5.99; P 12.93. $C_{10}H_{24}O_3NP$. Calculated %: N 5.91; P 13.08.

From the aqueous solution was isolated 0.8 g of diisoamylphosphoric acid.

3. Synthesis of di-n-hexyl amidophosphate (III). a) An aqueous solution of 5.8 g of chloramide was quickly added with stirring and cooling to 20 g of dihexyl phosphite. The temperature of the solution during addition rose from − 1 to + 3°. The reaction mass was subsequently stirred without cooling for 3.5 hours, and its temperature rose to 29° before slowly falling to room temperature (20°). The reaction product was extracted with ether and the extract washed with concentrated sulfuric acid, then with water until neutral, and dried with $MgSO_4$. Removal of the ether in vacuo left 17.45 g of dihexyl amidophosphate ($n^{20}D$ 1.4462, d^{20}_4 1.00537). The reaction product distilled over in presence of potassium carbonate, with slight decomposition, at 168-169° (0.23 mm) in the amount of 11.87 g ($n^{20}D$ 1.4452, d^{20}_4 0.9955).

Found for the undistilled substance %: N 5.36; P 11.4. Found for the distilled substance %: N 5.04; P 10.99. $C_{12}H_{28}PNO_3$. Calculated %: N 5.28; P 11.7.

From the aqueous solution was isolated 1.0 g of dihexylphosphoric acid.

* With participation of G. V. Gubin, V. M. Budanov, V. I. Teslin, and V. M. Portinov.

** Prepared by the procedure of [5] with the following modifications: To a prepared solution of hypochlorite was added 50 ml of 40% NaOH; before the start of the reaction 4-5 ml of concentrated ammonia (or 40-50 ml of 0.5 M solution) was run into the receiver; a vacuum of 25-30 mm was maintained in the system during the synthesis; the water bath temperature was 45-50°; the receiver was cooled with a mixture of ice and salt.

b) Di-n-hexyl chlorophosphate (VIII) was prepared by addition of 8.1 g of sulfuryl chloride to 15 g of di-n-hexyl phosphate in the course of 0.5 hour with ice cooling and with passage of dry air. After 2 hours' blowing with air, at room temperature, the mixture was distilled to give 13.5 g of di-n-hexyl chlorophosphate. B. p. 165-166° (8 mm), $n^{20}D$ 1.4381, d^{20}_4 1.0118.

Found %: Cl 12.3. $C_{12}H_{26}O_3PCl$. Calculated %: Cl 12.48.

Under the conditions of Expt. 1d, 7.1 g of di-n-hexyl chlorophosphate yielded 3.3 g (50%) of di-n-hexyl amidophosphate with b. p. 167-169° (0.3 mm).

4. Synthesis of pentoxyamidophenyl phosphonate (IV). Monoisoamylphenyl phosphonite (IX) was prepared by addition of 27 g of phenyldichlorophosphine (dissolved in an equal volume of absolute ether) to a mixture of 40 g of isoamyl alcohol, 15.2 g of triethylamine and 15 ml of ether with stirring at a temperature of − 8 to + 7°. The reaction mass was then stirred for 2 hours at room temperature, freed of hydrochloride and distilled to give 20.4 g of isoamylphenyl phosphonite with b. p. 138-139° (3 mm), $n^{20}D$ 1.5055, d^{20}_4 1.0502.

Found %: P 14.18. $C_{11}H_{17}O_2P$. Calculated %: P 14.62.

The substance decomposed when kept. Synthesis and distillation were performed in a carbon dioxide atmosphere.

Pentoxyamidophenyl phosphonate was prepared by the two routes described above. a) To 10.6 g of monoisoamylphenyl phosphonate was added, with cooling and stirring, a solution of 3.8 g of chloramide in 150 ml of water. The temperature of the reaction mixture rose from − 3 to + 4°. The reaction mass was then stirred for 3.5 hours without cooling, and its temperature rose to 6° above room temperature. The solid reaction product was washed with concentrated ammonia, then with water and dried. The resulting pentoxyamidophenyl phosphonate (7.4 g) was a yellowish powder with m. p. 68-74°, readily soluble in alcohols, ether, dioxane, ethyl acetate, chloroform, carbon tetrachloride, acetone and benzene; poorly soluble in water and very poorly in heptane. M. p. 76° after two recrystallizations from heptane.

Found %: N 6.28; P 13.56. $C_{11}H_{18}O_2NP$. Calculated %: N 6.17; P 13.66.

From the aqueous ammoniacal solution was isolated 0.6 g of pentoxyphenylphosphonic acid.

b) To 10.6 g of monoisoamylphenyl phosphonate was added 6.75 g of sulfuryl chloride in the course of 0.5 hour while a stream of dry carbon dioxide was passed through and the temperature was held at 5-15°. After being heated for 2 hours at 35-40°, the reaction mass was kept in vacuo for 2 hours. The resulting chlorophosphonate (a colorless liquid) was diluted with an equal volume of ether and saturated with dry ammonia (with cooling). After the ammonium chloride had been separated, the ether was driven off and the solid residue washed with heptane. Yield 6.8 g of amide with m. p. 50-56°. After four recrystallizations from heptane, pentoxyamidophenyl phosphonate melted at 75-76°.

Found %: N 6.50; P 13.21. $C_{11}H_{18}O_2NP$. Calculated %: N 6.17; P 13.66.

5. Synthesis of amidodiphenyl phosphonate (V). a) To 21.1 g of diphenylphosphinous acid in solution in 25 ml of benzene was added a solution of 7.5 g of chloramide in 170 ml of water. The procedure was similar to that of Expt. 1a except that stirring without cooling was continued for 4 hours, and the temperature of the reaction mass rose to 5° above room temperature. The reaction product was separated, washed with ammonia and then with water and dried. The amidodiphenyl phosphonate (10.8 g) melted at 146-150°. Readily soluble in alcohol, acetone, ethyl acetate and chloroform, less soluble in water, poorly soluble in benzene, ether and carbon tetrachloride. The pure compound had m. p. 160-161° (from benzene).

Found %: P 14.31; N 6.47. $C_{12}H_{23}O_3NP$. Calculated %: P 14.29; N 6.45.

Acidification of the aqueous solution yielded 8 g of diphenylphosphinic acid with m. p. 92° (from alcohol).

b) To 10.1 g of diphenylphosphinous acid dissolved in the minimum amount of dry benzene was added (with shaking) 6.75 g of sulfuryl chloride in an equal volume of benzene at a speed ensuring a temperature of the reaction mass of 35-40°. The resulting precipitate dissolved toward the end of the addition. After heating for an hour at 35-40°, the reaction mixture was kept in vacuo for 3 hours. The resulting chlorophosphonate (thick yellow liquid) was diluted with two volumes of benzene and saturated with dry ammonia. The precipitate

was collected and washed with benzene and then washed thoroughly with water. The amidodiphenyl phosphonate (2.35 g) melted at 158-160°; after recrystallization from benzene (1.13 g) it melted at 153-157°. No melting point depression in admixture with the amide prepared by the preceding method.

6. Synthesis of N-diethylamido-di-n-butyl phosphate (VI). a) To 10 g of dibutyl phosphite was added an ethereal solution of diethylchloramide at such a rate that the temperature did not rise above 35-40°; the mixture was afterward kept at that temperature for 2 hours. The ethereal solution was freed of hydrochloride, washed with water, alkali (10%) and again with water. It was then dried and fractionally distilled. Diethylamidodibutyl phosphate (2.4 g) came over at 128-140° (7 mm). Yield 18%.

b) To dibutyl chlorophosphate (0.1 mole) dissolved in dry ether was added diethylamine (0.2 mole) over a period of an hour with stirring and cooling. The reaction mass was heated for 1.5 hours at 40-45°, freed of hydrochloride and ether and fractionated. Diethylamido-di-n-butyl phosphate boiled at 136-137° (8 mm), $n^{20}D$ 1.4326, d^{20}_4 0.9659.

Found %: P 11.61; N 5.48. $C_{12}H_{28}O_3NP$. Calculated %: P 11.69; N 5.28.

7. Synthesis of N-diethylamido-diisoamyl phosphate (VII). a) The amidophosphate was obtained by the method of Expt. 6a in a yield of 20%; b. p. 140-150° (8 mm).

b) Diethylamido-diisoamyl phosphate was prepared by the procedure of Expt. 6b; b. p. 144-146° (8 mm); $n^{20}D$ 1.4320; d^{20}_4 0.9472.

Found %: P 11.08; N 5.35. $C_{14}H_{32}O_3NP$. Calculated %: P 10.65; N 4.78.

SUMMARY

1. A new reaction for conversion of the > POH grouping into the phosphamido group was studied.

2. Nine compounds not previously described were synthesized.

LITERATURE CITED

1. K. A. Petrov and G. A. Sokol'skii, Zhur. Obshch. Khim. 26, 3377 (1956).*
2. K. A. Petrov, G. A. Sokol'skii, and B. M. Polees, Zhur. Obshch. Khim. 26, 3381 (1956).*
3. K. A. Petrov and G. A. Sokol'skii, Zhur. Obshch. Khim. 26, 3378 (1956).*
4. B. A. Arbuzov, Reactions and Methods of Investigation of Organic Compounds [in Russian] (1954), pp. 7-72.
5. Inorganic Syntheses, Coll. Vol. 1, 61 (1951) [in Russian].

* Original Russian pagination. See C. B. translation.

STEROIDS

VI. SYNTHESIS OF CORTISONE ACETATE FROM PREGNANE-3(α), 17(α)-DIOL-11,20-DIONE

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Brief communications have recently been published in regard to the possibility of direct introduction of iodine into position 21 of 20-ketosteroids containing a Δ^4-3-keto- unsaturated grouping [1-3]. Preparation of Reichstein's substance S from 17 α-hydroxyprogesterone [4], of desoxycorticosterone acetate from progesterone [4], of 6-methylcortisone [5] and other compounds by direct iodination leads to a reduction in the number of steps in the syntheses of these preparations and presents considerable interest.

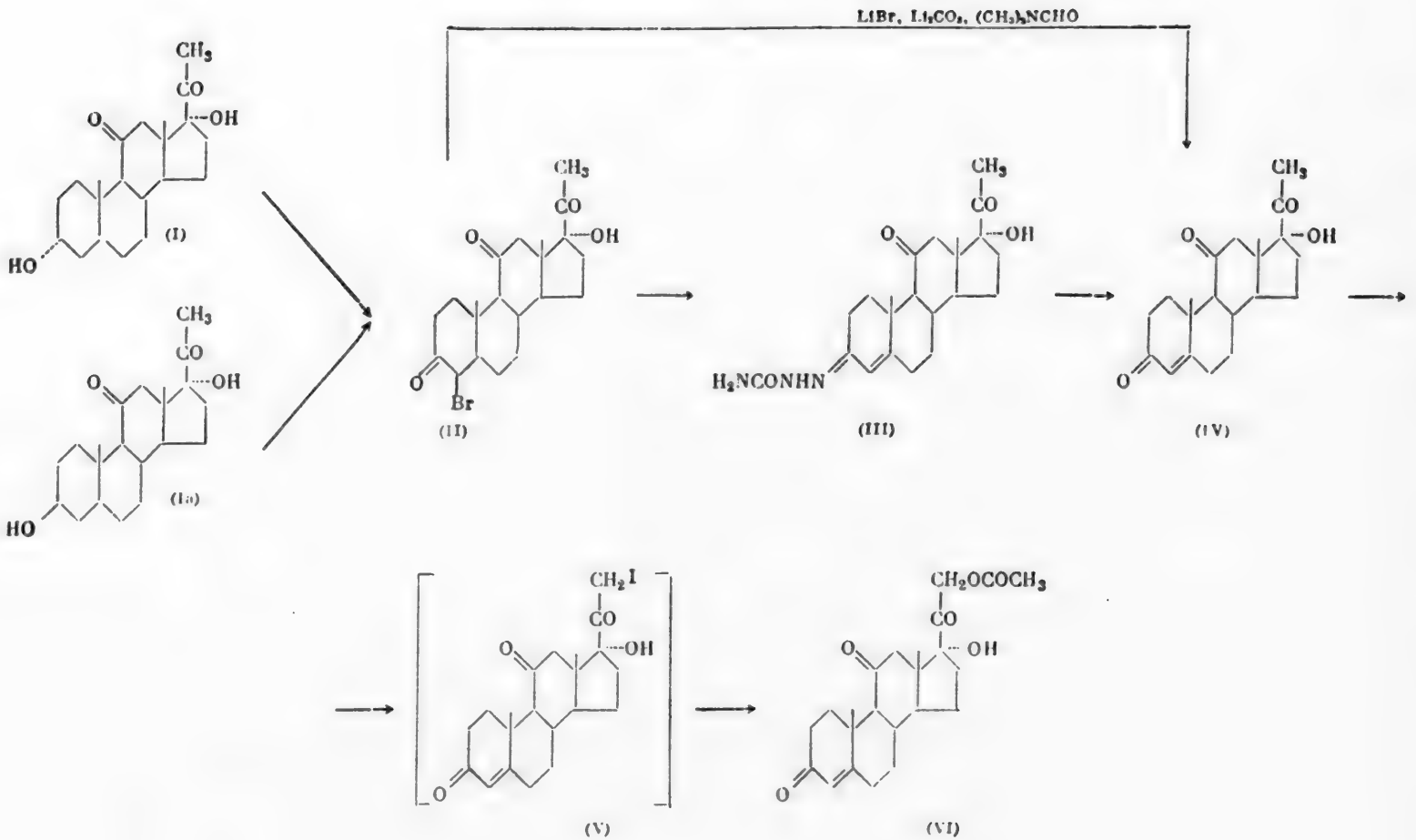
Our objective was the conversion of 3(α), 17(α)-diol-11,20-dione [6] (I) into Δ^4-17(α)-pregnenol-3,11,20-trione (IV) and the preparation from the latter of cortisone acetate by direct iodination in position 21 followed by replacement of the halogen by the acetoxy group.

Sarett [7] started from pregnane-3(α),17(α)-diol-11,20-dione (I) in the synthesis of Δ^4-pregnen-17(α)-ol-3,11,20-trione (IV). He oxidized (I) with chromic acid in acetic acid solution; the resulting trione was brominated with bromine to give 4-bromo-pregnan-17(α)-ol-3,11,20-trione (II) which was subjected to dehydrobromination by boiling with pyridine. In a later work [8] the oxidation of (I) to pregnan-17(α)-3,11,20-trione was effected with N-bromosuccinimide in tert-butanol in presence of water and pyridine; bromination and dehydrobromination with formation of Δ^4-pregnen-17(α)-ol-3,11,20-trione (IV) were performed under conditions similar to those of Sarett, and the yield of (IV) from the bromoketone was 53%.

The synthesis that we developed made use of the method of Hershberg and co-workers[9] of simultaneous oxidation and bromination. The latter oxidized 21-acetoxypregnane-3(α), 17(α)-diol-11,20-dione with N-bromosuccinimide in a mixture of tert-butanol and methylene chloride and obtained 4-bromo-21-acetoxy-pregnan-17(α)-ol-3,11,20-trione as the main product.

We therefore performed the synthesis of cortisone acetate (VI) from pregnane-3(α), 17(α)-diol-11,20-dione (I) by the following scheme.

Simultaneous oxidation and bromination of pregnane-3(α), 17(α)-diol-11,20-dione (I) by N-bromosuccinimide in methanol in presence of water and benzoyl peroxide gave 4-bromopregnan-17(α)-ol-3,11,20-trione (II) which was converted via the semicarbazone [6] followed by treatment with pyruvic acid [6, 10] into Δ^4-pregnen-17(α)-ol-3,11,20-trione (IV). We also effected direct transformation of (II) into (IV) by boiling the bromoketone in dimethylformamide with lithium salts [11, 12]; however the yield of (IV) and its melting point were then very much lower. Iodination of (IV) with excess of iodine in a mixture of tetrahydrofuran and methanol in presence of calcium oxide gave the 21-iodo derivative (V). The latter, without isolation in the pure state, was converted into cortisone acetate by boiling with potassium acetate in acetone. The product satisfied all pharmacopeal requirements after purification.


LiBr, Li2CO3, (CH3)2NCHO
CH3
CO
OH
O
HO
(I)
(Ia)
Br
(II)
H2NCONHN
(III)
(IV)
CH2I
(V)
CH2OCOCH3
(VI)

It was shown that performance of oxidation and bromination of the epimer of (I) – pregnane-3(β), 17(α)-diol-11,20-dione (Ia) – previously obtained by us [13] gave one and the same product (II). However, simultaneous oxidation and bromination of the β-epimer goes considerably faster and gives a higher yield of the desired product.

EXPERIMENTAL

4-Bromopregnan-17(α)-ol-11,20-dione (II). a) From pregnane-3(α), 17(α)-diol-11,20-dione (I). In a flask equipped with stirrer and mercury seal, thermometer and calcium chloride tube were placed 4 g of (I), 33 ml of methanol, 5.25 g of bromosuccinimide, 11.4 ml of water and 0.13 g of freshly precipitated benzoyl peroxide. The mixture was stirred at 20-21° for 6 hours, after which the reaction vessel was irradiated with a 25-watt lamp at a distance of 20 cm. After 20-30 minutes, the precipitate slowly began to dissolve and the reaction mixture turned yellow. A deep-orange, transparent solution was formed after $1\frac{1}{2}$ - 2 hours; the temperature rose spontaneously to 24-24.5° and then slowly fell to room temperature. Stirring was stopped after 6 hours and the reaction mixture was stood in the light for 42 hours. During this period the solution gradually lost its color and crystals came down. The latter were filtered and washed first with a few milliliters of aqueous methanolic sodium bisulfate and then with cold methanol and ether. The snow-white crystals were dried in a vacuum-desiccator over sulfuric acid until constant in weight (3.8 g). M. p. 185.5-186° (decomp.). The mother liquor was diluted with an equal amount of 1% sodium bisulfate solution in water and left for 10 hours in a refrigerator (+2°). The resulting precipitate was filtered, washed with water and dried in vacuo over sulfuric acid. Weight of substance collected 0.85 g. Two recrystallizations from dichloroethane gave 0.2 g of substance with m. p. 185°. Total yield of 4-bromopregnan-17(α)-ol-3,11,20-trione 4 g (81%); $[\alpha]^{20}D$ +69.8° (c 1, chloroform).

Found %: Br 18.70, 18.93. $C_{21}H_{29}O_4Br$. Calculated %: Br 18.78.

b) From pregnane-3(β), 17(α)-diol-11,20-dione (Ia). In a 1.3 ml flask with a ground-glass stopper were placed 41.3 mg of (Ia), 54 mg of bromosuccinimide, 1.5 ml of benzoyl peroxide, 0.4 ml of methanol and 0.05 ml of water. The flask was placed on a shaking machine and the contents agitated for 4 hours at room temperature (20°) while exposed to the light of a 25-watt electric lamp. The solid dissolved within 30 minutes after the start of the reaction and the solution acquired a deep-red color. The color nearly disappeared completely after an hour. Stirring was stopped after 4 hours; 0.05 ml of water was added (while the mass was rubbed with a small rod) and the mixture left for 12 hours to crystallize. The resulting crystals were filtered, washed with 0.1 ml of methanol and dried in a vacuum-desiccator over sulfuric acid. Weight of crystals 47 mg (93.2%).

After one recrystallization from dichloroethane the substance melted at 184°. Comparison of the infrared spectra of specimens of 4-bromopregnan-17(α)-ol-3,11,20-trione (II) obtained from pregnane-3(α), 17(α)-diol-11,20-dione (I) and pregnane-3(β), 17(α)-diol-11,20-dione (Ia) showed them to be completely identical.

3-Semicarbazone of Δ^4-pregnen-17(α)-ol-3,11,20-trione (III). To 3 g of (II) were added 156 ml of tert-butanol, 121 ml of anhydrous chloroform and 1 g of freshly recrystallized free semicarbazide. The flask was purged out with carbon dioxide and complete solution of the substances was effected by heating to 40° for 2-3 minutes on a water bath. The solution was allowed to stand for 2 hours at room temperature in daylight. The reaction mass quickly turned yellow but the color gradually disappeared in the course of 10-15 minutes. After 2 hours the whole of the solvent was taken off in vacuo in a nitrogen stream (bath temperature not higher than 35-40°). To the dry residue was added 104 ml of distilled water, the air in the flask was displaced by carbon dioxide, and the mixture was left in a refrigerator at +2° for 16 hours. The snow-white solid was filtered, thoroughly washed with water, and dried in a vacuum-desiccator over phosphorus pentoxide at room temperature until constant in weight (2.83 g). Yield quantitative.

Δ^4-Pregnen-17(α)-ol-3,11,20-trione (IV). To 2.83 g of (III) were added 85.5 ml of glacial acetic acid, 30.8 ml of water and 7.5 ml of 1.66 N aqueous pyruvic acid. The flask was purged out with carbon dioxide; the solution was heated on a water bath for 3 minutes to 45° and stood at room temperature for 24 hours. The solution, containing a small quantity of very fine crystals, was stirred dropwise into 550 ml of water cooled to 0°. The white crystals were filtered off and washed on the filter with a few milliliters of 2% sodium bicarbonate solution, then with water until neutral to litmus and finally with cooled methanol and ether. The product was dried in vacuo at 100° until constant in weight (1.95 g). After two recrystallizations from methanol the yield of Δ^4-pregnen-17(α)-ol-3,11,20-trione was 1.6 g (66%). M. p. 232.5-235°.

$[\alpha]^{23}D$ +182° (c 0.69, $CHCl_3$), λ_{max} 239 mμ (log ε 4.19).

Cortisone acetate (VI). To a solution of 0.8 g of (IV) in a mixture of 9 ml of tetrahydrofuran and 5.3 ml of methanol was added (in one portion) 1.2 g of iodine and 1.2 g of pulverized calcium oxide. The mixture was stirred at room temperature for 3 hours 15 minutes. After an hour, the color changed from dark-brown to light-yellow. The mixture was then stirred into 125 ml of iced water acidified with 5.2 ml of acetic acid. The calcium oxide dissolved and the solution turned bright-yellow. The reaction product was extracted (5 times) with methylene chloride; the extract was washed with water until neutral to litmus and dried with anhydrous sodium sulfate. The sulfate was filtered off and washed with dry methylene chloride. The solvent was completely driven off in vacuo at room temperature. The resulting 21-iodopregnen-17(α)-ol-3,11,20-trione (V) was dried in vacuo for an hour and dissolved in 125 ml of anhydrous acetone. To the solution was added 5 g of fused potassium acetate and the mixture boiled in a nitrogen stream with stirring for 20 hours. The greater part of the acetone was then distilled off and the residue was stirred into 250 ml of iced water containing 4 ml of sodium bisulfate. After half an hour the fine yellow crystals were filtered off, washed with cold water and carefully pressed on the filter. The wet precipitate was dissolved in 30 ml of ethanol, boiled with 0.3 g of active carbon for 10 minutes and filtered through a heated funnel. After standing for two hours at room temperature, the filtrate deposited small, yellowish needles which were filtered, washed with cooled ethanol and recrystallized again from ethanol and then from acetone. The product was dried for 8 hours at 100° in vacuo until constant in weight. There was obtained 0.2 g of cortisone acetate. M. p. 236-239°; $E^{1\%}_{1cm}$ 393.8; $[\alpha]^{20}D$ +182.3° (c 1, acetone).

The infrared spectrum of the substance was identical with the spectra of foreign specimens of cortisone acetate and with the spectrum of a preparation obtained from the All-Union Scientific Research Institute for Chemical Pharmaceutics.

The mother liquors from the recrystallizations of the main bulk of cortisone acetate were combined and evaporated in vacuo to a small volume. The resulting precipitate was filtered off and recrystallized to give 0.35 g with m. p. 232-235°. The technical cortisone acetate was dissolved in 150 ml of anhydrous benzene, and the solution chromatographed on 20 g of "SKh" adsorbent and eluted with benzene, ether and acetone. From the acetone fraction was isolated 0.2 g of cortisone acetate with m. p. 241°; $E^{1\%}_{1cm}$ 385.4. The infrared spectrum corresponded to that of specimens of the pure preparation. Total yield of cortisone acetate 0.4 g (43%, calculated on the Δ^4-pregnen-17(α)-ol-3,11,20-trione).

SUMMARY

1. A method was developed for simultaneous oxidation and bromination of pregnane-3(α),17(α)-diol-11,20-dione to give 4-bromopregnan-17(α)-ol-3,11,20-trione.

2. It was shown that oxidation and bromination of pregnane-3(α), 17(α)-diol-11,20-dione and of its epimer [pregnane-3(β), 17(α)-11,20-dione] with bromosuccinimide in methanol in presence of benzoyl peroxide leads to the same product — 4-bromopregnan-17(α)-ol-3,11,20-trione.

3. 4-Bromopregnan-17(α)-ol-3,11,20-trione was converted via the semicarbazone, followed by treatment of the latter with pyruvic acid, into Δ^4-pregnen-17(α)-ol-3,11,20-trione.

Cortisone acetate was obtained from Δ^4-pregnen-17(α)-ol-3,11,20-trione by direct iodination of the latter in position 21 followed by replacement of the iodine by the acetoxy group.

LITERATURE CITED

1. Chem. Age 79, 674 (1958).
2. Chem. Ing. News 11, 26 (1958).
3. British Patent 776,858 (1957); Chem. Abs. 52, 465 (1958).
4. H. Ringold and G. Stork, J. Am. Chem. Soc. 80, 250 (1958).
5. A. Bowers and H. Ringold, J. Am. Chem. Soc. 80, 3091 (1958).
6. N. N. Suvorov, Z. A. Yaroslavtseva, L. V. Sokolova, L. M. Morozovskaya, Zh. D. Ovchinnikova, V. S. Murasheva, F. Ya. Leibel'man, and M. A. Vorob'ev, Med. Prom. 2, 7 (1958).

7. L. Sarett, J. Am. Chem. Soc. 70, 1454 (1948).
8. T. Kritchevsky, D. Garmaise, and T. Gallacher, J. Am. Chem. Soc. 74, 483 (1952).
9. E. Hershberg, C. Gerold, and E. Oliveto, J. Am. Chem. Soc. 74, 3849 (1952).
10. E. Hershberg, J. Org. Ch. 13, 542 (1948).
11. R. Joly, J. Wernant, G. Nomine, and D. Bertin, Bull. Soc. Chim. 3, 366 (1958).
12. R. Joly and J. Wernant, Bull. Soc. Chim. 3, 367 (1958).
13. O. K. Nikiforova and N. N. Suvorov, Zhur. Obshch. Khim. 7, 1984 (1958).*

*Original Russian pagination. See C. B. translation.

ACYLATION OF ARENESULFAMIDES BY ESTERS OF ACETOACETIC ACID AND ITS DERIVATIVES

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Acyl derivatives of arenesulfamides are widely known and are usually synthesized by the action of acid anhydrides or chlorides on arenesulfamides [1]. Formyl and oxalyl derivatives of arenesulfamides were recently obtained [2] by the action of esters on alkali salts of sulfamides. It was of interest to ascertain the mode of reaction with alkali salts of arenesulfamides of esters of acids containing other functional groups.

In the present work we studied reactions of alkali salts of arenesulfamides with esters of acetoacetic acid and its derivatives. Reactants were benzene-, p-chlorobenzene- and p-toluenesulfamides and esters of acetoacetic and of chloro-, ethyl-, dichloro- and diethylacetoacetic acids. It was found that a mobile hydrogen present in the methylene group of the ester participates in the reaction with formation of the corresponding enolate.

$$ArSO_2NHNa + CH_3COCHXCOOEt \xrightarrow[-ArSO_2NH_2]{} CH_3C(ONa)=CXCOOEt$$

X = H, Cl, C_2H_5.

In the absence of a mobile hydrogen the ester grouping enters into reaction:

$$ArSO_2NHNa + CH_3COCl_2COOEt \xrightarrow[-EtONa]{} ArSO_2NHCOCCl_2COCH_3.$$

The reaction medium was boiling anhydrous methanol. The product could not be isolated pure due to the ease of hydrolysis in neutral and alkaline aqueous media with formation of arenesulfamides:

$$ArSO_2NHCOCCl_2COCH_3 \xrightarrow[-CH_3COCCl_2COOH]{+HOH} ArSO_2NH_2$$

In an organic acid medium, cleavage proceeds according to the equation:

$$ArSO_2NHCOCCl_2COCH_3 + HOH \xrightarrow[-CH_3COOH]{H^+} ArSO_2NHCOCHCl_2$$

Compounds prepared in this way were N-dichloroacetylbenzenesulfamide (I), N-dichloroacetyl-p-toluenesulfamide (II) and N-dichloroacetyl-p-chlorobenzenesulfamide (III). The products are colorless, crystalline substances, soluble in hot water and benzene; they titrate as one equivalent in the cold in presence of phenolphthalein.

A study of the reaction of arenesulfamides with diethylacetoacetic ester showed that this reaction does not take place either under the conditions applied for dichloroacetoacetic ester or at higher temperatures.

EXPERIMENTAL

Reaction of Na salt of benzenesulfamide. a) With acetoacetic ester. A mixture of 0.05 mole of the Na salt of benzenesulfamide (9 g), 0.05 mole of acetoacetic ester (16.5 g) and 15 ml of methanol was heated for 2 hours on a water bath. At the close of reaction the alcohol was taken off in vacuo and the residue treated with chloroform. The insoluble material (7 g) was recrystallized from benzene. No melting point depression in admixture with benzenesulfamide. The chloroform was distilled off from the solution in vacuo and the residue of syrupy liquid was acidified; acetoacetic ester separated. The residue titrated with acid.

Found M 160. $C_6H_7O_2NS$. Calculated M 152.

b) With chloroacetoacetic ester. A mixture of 0.01 mole of the Na salt of benzenesulfamide (1.79 g), 0.01 mole of chloroacetoacetic ester (1.64 g) and 15 ml of anhydrous methanol was heated on a water bath for 4 hours. The methanol was taken off in vacuo and the residue treated with chloroform. The insoluble portion (1.2 g) was recrystallized from benzene. A mixture with benzenesulfamide did not give a depression of melting point.

c) With dichloroacetoacetic ester. A mixture of 0.05 mole of Na salt of arenesulfamide (benzene 9 g, p-chlorobenzene 11.1 g, p-toluene 10.1 g), 0.05 mole of dichloroacetoacetic ester (10 g) and 15 ml of methanol was heated on a boiling water bath for 3 hours. The methanol was removed in vacuo. The syrupy residue crystallized after 2-3 days.

Found M 334. $C_{11}H_{11}O_4NSCl_2$. Calculated M 322.

Treatment of the syrup with 5 ml of formic acid led to formation of crystals which were dissolved in 5% sodium carbonate solution. Acidification of the solution gave a precipitate which was suction-filtered and recrystallized from benzene.

N-Dichloroacetylbenzenesulfamide, m. p. 150-151°. Yield 65.3%.

Found %: Cl 27.0; N 5.6. M 276. $C_8H_7O_3NSCl_2$. Calculated %: Cl 26.6; N 5.43. M 268.

N-Dichloroacetyl-p-toluenesulfamide, m. p. 139-141°. Yield 68.2%.

Found %: Cl 25.5. M 299.0. $C_9H_9O_3NSCl_2$. Calculated %: Cl 25.1. M 282.1.

N-Dichloroacetyl-p-chlorobenzenesulfamide, m. p. 174-176°. Yield 61.8%.

Found %: Cl 36.0; N 4.8. M 3120. $C_8H_6O_3NSCl_3$. Calculated %: Cl 35.2; N 4.64. M 302.5

SUMMARY

1. The reaction of alkali salts of arenesulfamides with esters of acetoacetic and chloro-, ethyl-, dichloro- and diethylacetoacetic esters was studied.

2. The following were synthesized: N-dichloroacetylbenzenesulfamide, N-dichloroacetyl-p-toluenesulfamide and N-dichloroacetyl-p-chlorobenzenesulfamide.

LITERATURE CITED

1. E. Noelting, Ber. 8, 598 (1875); N. T. Openschow and F. S. Spring, J. Chem. Soc. (1945), p. 284; T. W. Evans and W. M. Dehn, J. Am. Chem. Soc. 52, 1930 (1930); 51, 365 (1929); A. E. Kretov and A. I. Starikova, Ukr. Khim. Zhur. 24, 345 (1958); A. E. Kretov and M. M. Kremlev, Ukr. Khim. Zhur. 25, 482 (1959).
2. S. I. Burmistrov and G. E. Krakovtseva, Ukr. Khim. Zhur. 24, 349 (1958); S. I. Burmistrov, Ukr. Khim. Zhur. 24, 764 (1958).

SYNTHESIS OF THIAZOLE DERIVATIVES

XIV. NEW ALCOHOLS OF THE BENZOTHIAZOLE SERIES AND THEIR TRANSFORMATIONS

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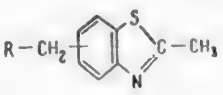
Among derivatives of 2-methylbenzothiazole not known until now were 2-methyl-5-hydroxymethyl- and 2-methyl-6-hydroxymethylbenzothiazoles (I) and (II). Their synthesis is described in the present communication. Starting substances were esters of 2-methylbenzothiazole-5- and 2-methylbenzothiazole-6-carboxylic acids. The methyl ester of the first of these acids was prepared from the methyl ester of 3-nitro-4-chlorobenzoic acid by the known method [1]; the ethyl ester of the second acid was synthesized from the acid chloride and alcohol. Conversion of the esters into carbinols (I) and (II) was effected by reduction with lithium aluminum hydride at − 40 and − 45° since at temperatures above 0° 2-methylbenzothiazole reacts with an ethereal solution of lithium aluminum hydride, probably at the double bond in the 1 position. Carbinols (I) and (II) may contain traces of the original ester; the latter is removed by treatment with alcoholic potassium hydroxide (the resulting potassium salts of benzothiazolecarboxylic acids are easily removed).

Synthesis of isomeric carbinols (I) and (II) opens up a route to preparation of a series of new derivatives of 2-methylbenzothiazole substituted in the 5 and 6 positions: chloromethyl-, cyanomethyl-, carboxymethyl-, diethylaminomethyl-, methoxymethyl- and acyloxymethyl-substituted derivatives.



(I & II) R=OH, (III & IV) R=Cl, (V & VI) R=CN, (VII & VIII) R=COOH, (IX & X) R=CH_3COO, (XI) R=C_6H_5COO, (XII) R=$N(C_2H_5)_2$, (XIII & XIV) R=CH_3O.

Bases (XII-XIV) are liquids, the others are colorless crystalline substances. Derivatives of 2-methylbenzothiazole with substituents in the 5 position are less soluble in organic solvents and more easily crystallized than their isomers with substituents in the 6 position. Under certain conditions the new bases form quaternary salts suitable for synthesis of cyanine dyes.

EXPERIMENTAL

2-Methyl-5-hydroxymethylbenzothiazole (I). A freshly prepared solution of 6.65 g (0.175 mole) of $LiAlH_4$ [2] in 335 ml of dry ether was placed in the reaction vessel of an apparatus cooled externally to − 50° by a solution of CO_2 in acetone. Dropwise addition with stirring was then made in the course of an hour of a solution of 20.7 g (0.1 mole) of the methyl ester of 2-methylbenzothiazole-5-carboxylic acid in 300 ml of dry ether. Stirring was continued at the same bath temperature for 50 minutes. Cooling was then stopped, and after the temperature inside the vessel had risen to − 15 to − 10° 150 ml of moist ether was run in with vigorous stirring, followed after 10 minutes by 100 ml of alkaline water. As soon as the ether layer had become transparent, it was poured off and the aqueous, syrupy residue extracted three times with ether. The ether extract

was dried with anhydrous Na_2SO_4, the solvent was driven off and the residual yellow, viscous oil dissolved in 40 ml of alcohol. The solution was mixed with a hot solution of 2 g NaOH in 25 ml of alcohol and the mixture heated for 5 minutes on a boiling water bath. The mass was then stood for 10 minutes for separation of the crystalline precipitate of the K salt of 2-methylbenzothiazole-5-carboxylic acid. The latter was filtered, washed with alcohol and benzene and used for separation of the acid. To the alcohol-benzene filtrate was added 100 ml of water and the liquid was extracted four times with benzene. The extract was dried with anhydrous Na_2SO_4 and the solvent was driven off to leave a yellowish or light-brown oil which soon crystallized. Yield 11-12.5 g (up to 70%). Further purification of (I) was effected by solution in 65 ml of ether, partial decolorization of the solution with carbon, concentration to a volume of 25 ml and cooling in a mixture of ice and salt. The crystals were then filtered and repeatedly washed with ligroine. Colorless, transparent needles with m. p. 59°.*

Found %: N 8.02, 7.94. C_9H_9ONS. Calculated %: N 7.82.

The methiodide was obtained in 82% yield by heating (I) with four times the quantity of methyl iodide in a sealed glass tube at 100° for 40 minutes. Colorless, finely crystalline powder; m. p. 226° (in a sealed capillary, from alcohol).

Found %: I 39.32. $C_{10}H_{12}ONSI$. Calculated %: I 39.56.

The ethiodide (I) was similarly obtained in 60% yield by heating the starting components for 4.5 hours. Colorless crystals with m. p. 180° (from alcohol) were obtained after washing with ether and acetone and recrystallization.

2-Methyl-6-hydroxymethylbenzothiazole (II). 2-Methylbenzothiazole-6-carboxylic acid was prepared from its nitrile [3]. A benzene solution of the acid chloride [4] was prepared from 45 g of the K salt of the acid and 16.8 ml of oxalyl chloride. The solvent was driven off, 100 ml of alcohol was run into the residue, and the mixture was heated to the boil and stood for several hours; it was then decolorized with carbon (2 g) and the alcohol distilled off from the filtrate. The solid product was pulverized and treated with 200 ml of saturated $NaHCO_3$ solution; the precipitate was filtered and washed with water. Yield 32 g. Yellowish-white crystals with m. p. 72° (from ligroine); the literature [3] gives the same melting point for the ester obtained by esterification of the acid.

Carbinol (II) was prepared in similar fashion to its isomer (I), starting from 11 g (0.05 mole) of ethyl ester of 2-methylbenzothiazole-6-carboxylic acid, dissolved in 200 ml of dry ether, and 115 ml of freshly prepared, sediment-free, solution of 3.3 g (0.087 mole) of $LiAlH_4$ in ether. During purification of (II) with an alcoholic solution of KOH, the K salt of 2-methylbenzothiazole-6-carboxylic acid does not separate due to its high solubility. Yield of (II) 7.6 g (85%). Colorless or slightly yellow, acicular crystals with m. p. 99° (from benzene).

Found %: N 7.65, 7.60; S 17.92, 17.90. C_9H_9ONS. Calculated %: N 7.82; S 17.88.

Methoiodide of (II): yield 93%; a colorless, finely crystalline powder with m. p. 182° (from alcohol).

Found %: I 39.27. $C_{10}H_{12}ONSI$. Calculated %: I 39.56.

Ethiodide: Yield 67%; fine, colorless needles with m. p. 185° (with decomp.) (from alcohol).

Found %: I 37.80, 37.66. $C_{11}H_{14}ONSI$. Calculated %: I 37.61.

2-Methyl-5-acetoxymethylbenzothiazole (IX). A mixture of 3.6 g of (I) and 20 g of acetic anhydride was boiled for 3 hours and the mixture poured into 150 ml of water. After an hour, it was cooled and the precipitate was filtered off and washed with water. Yield 3.5 g (81.5%); colorless, acicular crystals with m. p. 76° (from 30% alcohol).

Found %: N 6.26, 6.30. $C_{11}H_{11}O_2NS$. Calculated %: N 6.34.

2-Methyl-6-acetoxymethylbenzothiazole (X). Prepared from (II) as in the preceding preparation. The (X) separated by addition of water solidifies very slowly. Yield 3.1 g (70%); colorless needles with m. p. 47-48° (from 30% alcohol).

* Corrected melting and boiling points are given for all substances synthesized for the first time.

Found %: N 6.32, 6.27; S 14.47, 14.70. $C_{11}H_{11}O_2NS$. Calculated %: N 6.34; S 14.48.

2-Methyl-5-benzoyloxymethylbenzothiazole (XI). A mixture of 2.7 g (0.015 mole) of (I) and 2.25 g (0.016 mole) of benzoyl chloride was heated for 30 minutes at 105-110° (in a paraffin-wax bath). The reaction product was pulverized and treated with 35 ml of 3% NaOH solution, filtered, washed with water and dried. Yield 3.4 g (80%); colorless needles with m. p. 81° (from 50% alcohol).

Found %: N 4.98, 4.93. $C_{16}H_{13}O_2NS$. Calculated %: N 4.95.

2-Methyl-5-chloromethylbenzothiazole (III). To 13.8 g (0.66 mole) of PCl_5 and 75 ml of dry toluene was added 10.7 g (0.66 mole) of (I) with stirring. Heat was generated. When the temperature began to fall, the flask was placed in a paraffin bath heated to 110° and held at this temperature for 15 minutes. Heating was then interrupted and stirring was continued for another 30 minutes. Addition was made of 200 ml of 20% sodium carbonate solution (foaming occurred) and the mixture was stirred until complete solution took place. The toluene layer was separated and the aqueous layer extracted with toluene. The extract was dried with anhydrous sodium sulfate and partly decolorized by carbon; the solvent was then taken off (toward the end in the vacuum of a water jet pump). The residual light-brown oil quickly solidified. Yield 9.5-10.6 g. Long colorless needles with m. p. 78.5° (from ligroine). The chloro compound is not lachrymatory but irritates the skin slightly.

Found %: Cl 17.92, 17.94. C_9H_8NSCl. Calculated %: Cl 17.98.

2-Methyl-6-chloromethylbenzothiazole (IV). From 3.6 g of (II) and 4.6 g of PCl_5 was obtained 3.0 g (76%). Colorless needles with m. p. 86° (from ligroine).

Found %: Cl 17.89, 17.92. C_9H_8NSCl. Calculated %: Cl 17.98.

2-Methyl-5-cyanomethylbenzothiazole (V). To a mixture of 3.3 g (0.05 mole) of KCN and 2 ml of water was added a warm solution of 7.9 g (0.04 mole) of (III) in 20 ml of alcohol and the mass was heated on a boiling water bath for 4 hours. The precipitated KCl was filtered off and washed with a little alcohol. The filtrate was partly decolorized with carbon and concentrated to a volume of 12 ml. After cooling in ice, the precipitate was filtered and washed with a little alcohol and then several times with water. Yield 6.5 g (81.7%). Colorless, transparent, lustrous, hexagonal tablets with m. p. 106° (from alcohol).

Found %: N 14.80, 14.61. $C_{10}H_8N_2S$. Calculated %: N 14.89.

2-Methyl-6-cyanomethylbenzothiazole (VI). Starting components for synthesis were 3.5 g of (IV) and 1.45 g of KCN. After the KCl had been removed and the aqueous alcoholic solution had been concentrated to a volume of 5 ml, 35 ml of water was added and the mass was cooled. Compound (VI) separated as an oil which quickly solidified. It was filtered off and washed with water. Yield 3.0 g (91%); fine, colorless crystals with m. p. 76° (from 70% alcohol).

Found %: N 14.69, 14.55. $C_{10}H_8N_2S$. Calculated %: N 14.89.

2-Methyl-5-carboxymethylbenzothiazole (VII). A mixture of 6 g (0.032 mole) of (V) and 15 ml of HCl (d 1.19) was heated for 5 hours at 140° in two sealed glass tubes. No pressure was detected when the tubes were opened. The contents of the tubes were mixed with 75 ml of 10% NaOH solution, heated and decolorized with carbon. Dilute HCl was added to the warm filtrate until the liquid had a weakly acidic reaction. It was then cooled. The white, finely crystalline precipitate of (VII) was filtered off and washed with water. Yield 6.15 g (92.7%); colorless needles with m. p. 198° (from alcohol).

Found %: N 6.99, 7.01. $C_{10}H_9O_2NS$. Calculated %: N 6.76.

2-Methyl-6-carboxymethylbenzothiazole (VIII). From 3.8 g of (VI) was obtained (by the preceding method) 3.8 g of (VIII) (91.7%). Colorless, lustrous, fine plates with m. p. 203.5° (from 33% alcohol).

Found %: N 6.94; S 15.61. $C_{10}H_9O_2NS$. Calculated %: N 6.76; S 15.46.

2-Methyl-5-methoxymethylbenzothiazole (XIII). To a solution of sodium methoxide, prepared from 0.46 g (0.02 g-atom) of sodium and 15 ml of absolute methanol, was added a warm solution of 3.95 g (0.02 mole) of (III) in 15 ml of the same solvent, and the mixture was boiled for 45 minutes. The NaCl was filtered off and washed with methanol. The greater part of the solvent was driven off from the filtrate. Addition of 10 ml of water led to separation of an oil which was extracted with ether; the extract was dried with anhydrous

Na_2SO_4, the ether was driven off and the residue distilled in vacuo. Yield 3 g (77.7%). A colorless, oily liquid with a characteristic faint odor; b. p. 136° at 6 mm.

Found %: N 7.13, 7.25. $C_{10}H_{11}ONS$. Calculated %: N 7.25.

2-Methyl-6-methoxymethylbenzothiazole (XIV). a) The synthesis was carried out as for the preceding preparation, starting from 2.4 g of (IV) and 2.3 g of sodium. Yield 1.7 g (73%); b. p. 145-146° at 8.5 mm; a colorless, viscous, strongly refracting liquid with a very weak odor.

Found %: N 7.06, 7.12. $C_{10}H_{11}ONS$. Calculated %: N 7.25.

b) A mixture of 5.4 g (0.03 mole) of the methyl ether of p-acetylaminobenzyl alcohol, 3.4 g (0.015 mole) of P_2S_5 and 30 ml of dry toluene was heated for 10 minutes at 120°. The viscous mass was extracted with toluene. The thioacetyl derivative was extracted from the toluene with 100 ml of 20% NaOH solution. The alkaline solution was treated, while cooling, with acetic acid until it turned cloudy and CO_2 was released. It was then extracted with chloroform. The solvent was distilled off from the extract (after drying with Na_2SO_4). Two g of the resulting thioacetyl derivative was mixed at 5° with 18 ml of 10% NaOH solution and with a solution of 9.2 g of potassium ferricyanide in 52 ml of water. After 20 hours, the mixture was distilled with steam and the distillate extracted with ether. The extract was dried with anhydrous Na_2SO_4 and the solvent was driven off to leave 1.2 g (60%) of (XIV). B. p. 143-145° at 7 mm.

Methyl ether of p-aminobenzyl alcohol. p-Nitrobenzyl bromide was prepared by bromination of p-nitrotoluene with dibromodimethylhydantoin [5]; yield of bromo derivative 65%, m. p. 96° (from methanol). The methyl ether of p-nitrobenzyl alcohol was synthesized from p-nitrobenzyl bromide and sodium methoxide on similar lines to its preparation from p-nitrobenzyl chloride [6]; yield 91%, b. p. 145° at 14 mm.

Into a hydrogenation flask were charged 0.1 g of platinum oxide [7], 70 ml of 96% alcohol and 10 g (0.06 mole) of the methyl ether of p-nitrobenzyl alcohol. Hydrogenation was carried out for 4 to 6 hours and led to uptake of 4.2-4.4 liters of hydrogen and to disappearance of the yellow color of the solution. The same portion of catalyst was used 2-3 times. The solution of hydrogenation product was decanted from the catalyst and the alcohol distilled off (the last traces were removed in the vacuum of a water jet pump). Yield 7.5 g (91%).

Methyl ether of p-acetylaminobenzyl alcohol. A mixture of 7.5 g of methyl ether of p-aminobenzyl alcohol and 20 ml of acetic anhydride was run (after 20 minutes' mixing) into 60 ml of water, stirred, and cooled in ice. The yellowish crystals were washed with water. Yield 6.5 g (66.3%). Colorless crystals with m. p. 108° (from water).

Found %: N 7.90, 7.85. $C_{10}H_{13}O_2N$. Calculated %: N 7.82.

2-Methyl-5-dimethylaminomethylbenzothiazole (XII). A mixture of 1.2 g (0.006 mole) of (III), 1.3 g (0.018 mole) of diethylamine and 5 ml of absolute alcohol was boiled for 15 minutes and stood for 20 hours. Excess of dry ether was added and the mass was cooled. The precipitate of diethylamine hydrochloride was filtered off. The ether-alcohol filtrate was treated with KOH powder, the solvent was taken off, water was added to the residue and the latter was extracted with benzene. The benzene was driven off and the residue distilled in vacuo to give 1.2 g of product (85.7%); b. p. 152° at 5 mm. A colorless, viscous liquid with a very faint amine odor.

Found %: N 12.22, 12.23. $C_{13}H_{18}N_2S$. Calculated %: N 11.97.

Picrate: m. p. 135° (from alcohol).

SUMMARY

Reduction of esters of 2-methylbenzothiazole-5- and 2-methylbenzothiazole-6-carboxylic acids by lithium aluminum hydride gave new alcohols of the benzothiazole series — 2-methyl-5-hydroxymethyl- and 2-methyl-6-hydroxymethylbenzothiazoles. The alcohols were used for synthesis of twelve derivatives of 2-methylbenzothiazole substituted in positions 5 or 6 by chloromethyl, cyanomethyl, carboxymethyl, methoxymethyl, diethylaminomethyl and acyloxymethyl groups.

LITERATURE CITED

1. U. S. Patent 2,647,051; Chem. Abs. 47, 11056g (1953).
2. A. E. Finholt, A. C. Bond, and H. I. Schleisinger, J. Am. Chem. Soc. 69, 1199 (1947).
3. I. K. Ushenko, Dissertation, Institute of Organic Chemistry, Acad. Sci. UkrSSR (1943).
4. H. Wingfield, W. Harlan, and H. Hammer, J. Am. Chem. Soc. 75, 4364 (1953); V. M. Zubarovskii, Zhur. Obshch. Khim. 24, 1665, 1661, 1671 (1954).*
5. O. Orazi and J. Meseri, Ann. Assoc. Chim. Argentina 38, 187 (1950); Chem. Abs. 45, 561 (1951).
6. G. Romeo, Gazz. 35, 1, 111 (1905).
7. Syntheses Org. Prep. 1, 357 (1949).

* Original Russian pagination. See C. B. translation.

OXIDATION OF 1-PHENYL-1-CYCLOPENTENE BY PERFORMIC ACID AND THE SYNTHESIS OF 1-METHYL- AND 1-ETHYL-2-PHENYLCYCLOPENTANE

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During investigation of the composition of the components of a series of petroleums it was found that the ligroine-kerosene and higher fractions contained not only paraffinic, naphthenic and aromatic hydrocarbons but also hydrocarbons containing both aromatic and naphthenic rings. In their properties these hydrocarbons are intermediate between naphthenes and aromatics. Only a small number of hydrocarbons of this type had previously been synthesized. The lack of standards hinders the successful employment of spectral methods in the investigation of such compounds in oil fractions.

Among the known hydrocarbons containing a cyclopentane and a benzene ring are many α-cyclopentyl-ω-phenylalkanes, also 1-methyl-2-(β-phenylethyl)-cyclopentane, 1-methyl-2-(γ-phenylpropyl)-cyclopentane [1] and some products of condensation of alkyl-, dialkyl- and trialkylbenzenes with cyclopentene [2]. The position of the cyclopentyl substituent in the benzene in the majority of these compounds has not been established. It is also reported that 1-methyl-2-phenylcyclopentane was obtained by dehydrogenation of 1-methyl-2-cyclohexylcyclopentane over palladized carbon at 410°. However, this hydrocarbon was not isolated from the catalyzate which still contained 21% of the original hydrocarbon. The density and refractive index of 1-methyl-2-phenylcyclopentane were only determined by extrapolation [3].

The first two members of the 1-alkyl-2-phenylcyclopentane series are described in this paper as a sequel to an investigation of the synthesis of some 1,2-dialkylcyclopentanes containing 10 to 13 carbon atoms [4]. The oxidation of 1-phenyl-1-cyclopentene by performic acid was studied with the objective of obtaining the starting substance – 2-phenyl-1-cyclopentanone.

There are very few literature data on this problem. Oxidation of 1-phenyl-1-cyclopentene with performic acid (from 98% formic acid and 27% hydrogen peroxide) at below 45° gave mainly γ-benzoylbutyric acid (yield 64%) together with a certain amount of 2-phenyl-1-cyclopentanone (yield not stated) [5]. Oxidation with sulfuric acid of 1-phenyl-1,2-cyclopentanediol monoformate (obtained by oxidation of 1-phenyl-1-cyclopentene by performic acid) gave 2-phenyl-1-cyclopentanone-1 (yield 75-80%) [6]. However, the conditions of hydrolysis of the monoformate were not specified and it is not certain whether the monoformate was formed at all since its constants are not given. In general it would be expected that oxidation of 1-phenyl-1-cyclopentene by performic acid and subsequent hydrolysis of the monoformate would lead to formation of trans-1-phenyl-1,2-cyclopentanediol [7] which has not been described in the literature.

We carried out the oxidation of 1-phenyl-1-cyclopentene with performic acid (prepared from 85% formic acid and hydrogen peroxide) [8]. We see from Table 1 that even a rise of temperature of a few degrees (Expts. 1 and 2) leads to a considerable fall in yield of 1-phenyl-1-cyclopentene (from 66 to 40%) and to an appreciable increase in yield of γ-benzoylbutyric acid (from 8 to 14%). Lowering of the concentration of the hydrogen peroxide to 19% (Expt. 3) and lowering of the reaction temperature to 23-24° lead to a sharp fall in yield of

ketone (29%). At the same time the yield of ketoacid remains high, probably due to further oxidation of the ketone formed. The reaction mass contains up to 30% of unreacted hydrocarbon. It should be noted that even under such relatively mild oxidation conditions, neither the glycol nor its monoformate nor the α-oxide could be isolated.

TABLE 1

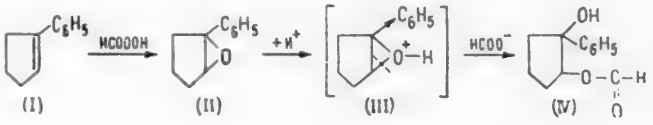
Oxidation of 1-Phenyl-1-cyclopentene by Performic Acid

Expt. No.	H_2O_2 concentration (in %)	Reaction temperature	Yield (in %)	
			of ketone	of ketoacid
1	27	30—35°	66.3	8.3
2	27	35—42	40.2	14.3
3 *	19 (without excess)	23—24	29.3	23.2

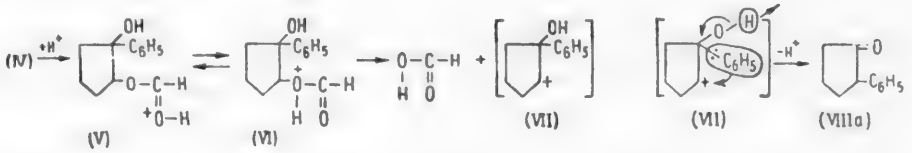
* 0.125 mole of hydrocarbon was oxidized as against 0.5 mole in the other experiments. In this experiment 30% of the hydrocarbon did not react.

In the present case the initial product of peracid oxidation of 1-phenyl-1-cyclopentene [9] ought to be the α-oxide, but 2-phenyl-1-cyclopentanone could be formed from the latter by isomerization [5, 10] or, following the addition of acid, via the glycol monoformate and hydrolysis of the monoformate [8]. The mechanism of isomerization of α-oxides to aldehydes and ketones [11] has not been adequately studied. It has been suggested that the first step is addition of acid to α-oxide with formation of glycol monoester and that the latter undergoes hydrolysis and splits off acid [12]. Hence, the acid hydrolysis of monoesters lies at the basis of the isomerization of α-oxides and is the main step in formation of ketones during oxidation of unsaturated compounds by peracids. It may be expected that opening of the α-oxide ring of 1-phenyl-1-cyclopentene in presence of acid would be accompanied by rupture of the bond between the oxygen atom and the more hydrogenated carbon atom due to the negative inductive effect of the phenyl group [13]. This is true of the opening of the α-oxide ring of styrene oxide under the action of formic or acetic acid [10].

Formation of 1-phenyl-1,2-cyclopentanediol monoformate by oxidation of 1-phenyl-1-cyclopentene with performic acid can accordingly be represented as follows:



In a strongly acid medium the resulting glycol monoformate is converted into 2-phenyl-1-cyclopentanone. This process can evidently be represented by the following sequence of reactions on the basis of the mechanism of acid hydrolysis of esters [14]:



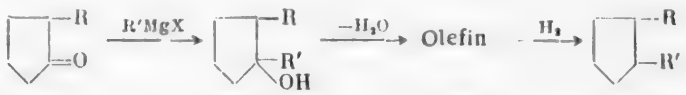
In an acid medium a proton joins on to the carbonyl oxygen with formation of cation (V) which then changes to its tautomer (VI). Cation (VI) then breaks down to formic acid and carbonium ion (VII), which undergoes pinacolone rearrangement to 2-phenyl-1-cyclopentanone (VIIIa).

It should be noted that, unlike monoformates of 1-alkyl-1,2-cyclopentanediols which are stable in an acid medium under conditions of oxidation of 1-alkyl-1-cyclopentenes (40-45°) and are hydrolyzed mainly only at above 100° [8], 1-phenyl-1,2-cyclopentanediol is hydrolyzed in an acid medium even during mild oxidation (at 23-24°).

Fairly large quantities of γ-benzoylbutyric acid are formed in all experiments on oxidation of 1-phenyl-1-cyclopentene, and it was therefore of interest to establish whether the acid is formed directly during performic acid oxidation of the hydrocarbon or whether it is the product of further oxidation of 2-phenyl-1-cyclopentanone. The sole product of oxidation of 2-phenyl-1-cyclopentanone by performic acid actually proved to be γ-benzoylbutyric acid (yield 64.2%). We know from the literature that 2-phenyl-1-cyclopentanone [15, 16] and 2-phenyl-1-cyclohexanone [17] are easily oxidized to the corresponding ketoacids even by oxygen of the air.

The main product of oxidation of 1-phenyl-1-cyclopentanol with performic acid was a substance with the formula $C_{22}H_{26}O_2$ and m. p. 83°; there were also isolated a phenolic substance with m. p. 37°, which was not further examined, and a small quantity of 2-phenyl-1-cyclopentanone.

1-Methyl- and 1-ethyl-2-phenylcyclopentanes were synthesized by the following route:



(VIII) (IX) (X) (XI)

(VIII, IX, XI) a) R = C_6H_5; b) R = CH_3; c) R = C_2H_5.

(IX, XI) a) R' = CH_3 (X = I); b) R' = C_6H_5 (X = Br); c) R' = C_6H_5 (X = Br).

1-Methyl-2-phenyl-1-cyclopentanol (IXa) and 1-ethyl-2-phenyl-2-cyclopentanol (IXc) were prepared by Grignard reaction from, respectively, 2-phenyl-1-cyclopentanone and methylmagnesium iodide and 2-ethyl-1-cyclopentanone and phenylmagnesium bromide. The respective yields were 70 and 76%. 1-Methyl-2-phenyl-2-cyclopentanol, prepared by reaction of 2-methyl-1-cyclopentanone and phenylmagnesium bromide, was not isolated because it underwent complete dehydration in course of fractional distillation. Tertiary alcohols (IXa) and (IXc) were obtained in the form of a mixture of cis- and trans-isomers which were not separated. These alcohols have been dehydrated by saturated oxalic acid solution [18]. Unsaturated hydrocarbons (X) from 1-methyl-2-phenyl-1-cyclopentanol and 1-ethyl-2-phenyl-2-cyclopentanol were obtained in yields of 78 and 72%, while 1-methyl-2-phenyl-1-cyclopentene was obtained in 70% yield (on the original ketone) without separation of 1-methyl-2-phenyl-2-cyclopentanol.

Dehydration of the tertiary alcohols can take two courses with formation of unsaturated hydrocarbons of different types but having one and the same carbon framework.

(XII) (XIII)

a) R' = CH_3, R = C_6H_5; b) R' = C_6H_5, R = CH_3; c) R' = C_2H_5, R = C_6H_5.

Complete separation of these hydrocarbons was not effected due to the closeness of their boiling points; only fractions enriched with one isomer or the other were obtained. Mixtures of isomers were subjected to hydrogenation in presence of palladium black in alcoholic solution at room temperature. One and the same saturated hydrocarbon was obtained. The resulting 1-methyl- and 1-ethyl-2-phenylcyclopentanes were distilled in vacuo in an 80-plate metal-packed column. The distilled hydrocarbons were found to be individual substances, whereas the synthesis of 1,2-dialkylcyclopentanes gave a mixture of isomers in which the trans-forms greatly predominated (81-83%) over the cis-forms [1]. Constants of the synthesized hydrocarbons are given in Table 2.

EXPERIMENTAL

Oxidation of 1-phenyl-1-cyclopentene by performic acid. 1-Phenyl-1-cyclopentene (b. p. 75-76° at 3 mm, m. p. 20.1°) was obtained in 93.2% yield by dehydration with saturated oxalic acid of 1-phenyl-1-

cyclopentanol (b. p. 101-102° at 3 mm, m. p. 13.2°, $n^{20}D$ 1.5488, d^{20}_4 1.0566) and was oxidized with a mixture of 85% formic acid (13.2 moles per mole of hydrocarbon) and 27 and 19% of hydrogen peroxide (approximately 1.5 moles per mole of hydrocarbon) at 23-24° and 30-42°. Oxidation results are set forth in Table 1.

TABLE 2

Constants of 1-Methyl- and 1-Ethyl-2-phenylcyclopentanes

Hydrocarbon	Boiling point		n_D^{20}	d_4^{20}	MR_D	
	at 30 mm	recalc. at 760 mm			found	calc.
1-Methyl-2-phenylcyclopentane[b]	121.7°	229.6°	1.5238	0.9414	52.07	51.82
1-Ethyl-2-phenylcyclopentane[c]	136.8	247.8	1.5217	0.9378	56.65	56.43

Remarks. Both hydrocarbons became vitreous when cooled.

a. Temperatures were converted by tables [23] for hydrocarbons of the cyclopentane and benzene series and the mean of both values was taken.

b. Found %: C 89.91, 89.88; H 9.93, 10.09. $C_{12}H_{16}$. Calculated %: C 89.93; H 10.07.

c. Found %: C 89.28, 89.28; H 10.21, 10.20. $C_{13}H_{18}$. Calculated %: C 89.59; H 10.41.

Compare constants of 1-methyl-2-phenylcyclopentane, $n^{20}D$ 1.5430, d^{20}_4 0.941, obtained by extrapolation [3].

Yield of 2-phenyl-1-cyclopentanone 183.3 g; b. p. 115-116° (3 mm), m. p. 34.5°. Literature data [16]: b. p. 96° (0.4 mm), m. p. 36.5-37.5°.

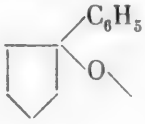
Semicarbazone: m. p. 220-221° (decomp.). Literature: m. p. 213-214° [19], 231-232° [6].

γ-Benzoylbutyric acid: m. p. 129-130° (from water). Literature [20]: m. p. 128-129°.

Semicarbazone: m. p. 212° (decomp.). Literature [21]: m. p. 212-213°.

Oxidation of 1-phenyl-1-cyclopentanol. Oxidation of 20.2 g of 1-phenyl-1-cyclopentanol was effected with performic acid (using 19% hydrogen peroxide) at 38-44° in the above fashion. Crystals came out on the following day (11.2 g) and were filtered off; m. p. 83°. Formic acid and water were distilled off from the filtrate and the residue was distilled in vacuo to give 0.95 g of a substance with b. p. 45-47° (2 mm) (it crystallized and had m. p. 37°) and 2.8 g of 2-phenyl-1-cyclopentanone; semicarbazone m. p. 220-221° (decomp.).

The compound with m. p. 37° gave all the qualitative reactions for phenols; it was not further investigated.

The nature of the crystalline substance with m. p. 83° was not established. Analytical data and molecular weight determination indicate that it contains two  residues; it does not give reactions characteristic of acids, peroxides, tertiary alcohols or carbonyl compounds.

Found %: C 81.79, 81.89; H 8.10, 8.19. M 298.5, 309.75. $C_{22}H_{26}O_2$. Calculated %: C 81.95; H 8.13. M 322.4.

Oxidation of 2-phenyl-1-cyclopentanone. Oxidation of the ketone (10.5 g) was effected under conditions similar to those for oxidation of 1-phenyl-1-cyclopentanol. There were obtained 7 g (64.2%) of γ-benzoylbutyric acid and 1.4 g of unreacted ketone.

1-Methyl-2-phenyl-1-cyclopentanol (IXa) was prepared by Grignard reaction from 87.8 g (0.55 mole) of 2-phenyl-1-cyclopentanone and methylmagnesium iodide [from 17 g (0.7 mole) of magnesium and 98 g (0.7 mole) of methyl iodide]. Yield 67.6 g (70%); b. p. 98-114° (3 mm). The alcohol consisted of a mixture of cis- and trans-isomers which were not separated.

1-Methyl-2-phenylcyclopentene. Dehydration of 61 g of 1-methyl-2-phenyl-1-cyclopentanol was effected with saturated oxalic acid solution [18]. A total of 42.9 g (78.4%) of unsaturated hydrocarbons (XIIa) and (XIIIa) was obtained.

1-Methyl-2-phenyl-2-cyclopentanol (IXb). Prepared by Grignard reaction from 145.4 g (1.48 moles) of 2-methyl-1-cyclopentanone and phenylmagnesium bromide [from 40.5 g (1.66 moles) of magnesium and 262 g (1.66 moles) of bromobenzene]. The product was worked up in the usual manner. On fractionation in vacuo the alcohol was completely dehydrated and was not isolated. The resulting 1-methyl-2-phenylcyclopentene was redistilled over metallic sodium; yield 164.6 g (70.2% on the original ketone). The hydrocarbon comprised a mixture of the two possible isomers (XIIb) and (XIIIb) which were not separated. Two fractions were obtained enriched with one isomer or the other. The fractions had the following characteristics:

1st, b. p. 66-66.5° (2 mm), $n^{20}D$ 1.5603, d^{20}_4 0.9651, MR_D 53.04. $C_{12}H_{14}F_4$. Calculated 51.35.

Found %: C 90.98, 91.09; H 8.97, 8.84. $C_{12}H_{14}$. Calculated %: C 91.09; H 8.92.

2nd, b. p. 67.3-67.5° (2 mm), $n^{20}D$ 1.5617, d^{20}_4 0.9668, MR_D 53.05. $C_{12}H_{14}F_4$. Calculated 51.35.

Found %: C 90.75, 90.72; H 8.84, 8.89. $C_{12}H_{14}$. Calculated %: C 91.08; H 8.92.

The large increment of molecular refractions of both fractions of unsaturated hydrocarbons is evidently associated with conjugation between the double bond and the benzene ring.

1-Methyl-2-phenyl-2-cyclopentene is described in the literature: b. p. 116-117° (20 mm) [22].

1-Methyl-2-phenylcyclopentane was prepared by separate hydrogenation of 41.2 g of unsaturated hydrocarbons (obtained from 1-methyl-2-phenyl-1-cyclopentanol) and 131.8 g of unsaturated hydrocarbons (obtained from 1-methyl-2-phenyl-2-cyclopentanol) in alcoholic solution at room temperature in presence of palladium black. Both preparations had identical constants and were combined. The hydrocarbon was distilled over sodium and fractionated in an 80-plate, metal-packed column in vacuo. Constants are given in Table 2.

1-Ethyl-2-phenyl-2-cyclopentanol (IXc). Prepared by Grignard reaction from 140.2 g (1.25 moles) of 2-ethyl-1-cyclopentanone and phenylmagnesium bromide [from 32.7 g (1.34 moles) of magnesium and 210.4 g (1.34 moles) of bromobenzene]; yield 181.6 g (76.4%), b. p. 114° (4.5 mm), 121° (3 mm). The alcohol was obtained in the form of a mixture of stereoisomers whose separation was not undertaken.

1-Ethyl-2-phenylcyclopentene was prepared by dehydration of 174.8 g of 1-ethyl-2-phenyl-2-cyclopentanol (yield 114.5 g or 72.4%) in the form of a mixture of the two possible isomers (XIIc) and (XIIIc):

B. p. 94.5-95° (4 mm), $n^{20}D$ 1.5522, d^{20}_4 0.9588; MR_D 57.42. $C_{13}H_{16}F_4$. Calculated 55.97.

Found %: C 90.75, 90.54; H 9.54, 9.17. $C_{13}H_{16}$. Calculated %: C 90.64; H 9.36.

1-Ethyl-2-phenylcyclopentane was prepared by hydrogenation of 98 g of 1-ethyl-2-phenylcyclopentene. Constants are shown in Table 2.

SUMMARY

1. A study was made of the oxidation of 1-phenyl-1-cyclopentene by performic acid. It was shown that the main products of oxidation are 2-phenyl-1-cyclopentanone and γ-benzoylbutyric acid. Contrary to experience with 1-alkyl-1-cyclopentenes, it was not possible to isolate the monoformate of 1-phenyl-1,2-cyclopentanediol from the products of oxidation of 1-phenyl-1-cyclopentene.

2. Oxidation of 2-phenyl-1-cyclopentanone under the same conditions leads exclusively to formation of γ-benzoylbutyric acid.

3. 1-Methyl-2-phenylcyclopentane and 1-ethyl-2-phenylcyclopentane were synthesized for the first time.

LITERATURE CITED

1. Ya. I. Denisenko and A. D. Nabar, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk 35 (1945).
2. E. S. Pokrovskaya, Doklady Akad. Nauk SSSR 39, 26 (1943); Trudy Inst. Nefti Akad. Nauk SSSR 1, 264 (1950).
3. R. Sperling, J. Chem. Soc. (1949), p. 1928.
4. A. F. Platé, A. A. Mel'nikov, R. A. Zelenko, and N. I. Lykova, Doklady Akad. Nauk SSSR 123, 1044 (1958).*
5. J. P. Vila and R. Crespo, Anal. real. soc. Espan. fis. y. quim. 48B, 273 (1952); Chem. Abs. 47, 3802 (1953).
6. M. Mousseron, R. Jacquier, and H. Christol, Compt. rend. 236, 927 (1953).
7. P. E. Verkade and J. Coops, Jr., Chr. J. Maan, and A. Verkade-Sandbergen, Lieb. Ann. 467, 217 (1928); J. Böeseken, Ber. 56, 2409 (1923).
8. A. F. Platé and A. A. Mel'nikov, Zhur. Obshch. Khim. 30, 927 (1960).*
9. Org. Reactions, Coll. 7, 476 (1956).
10. W. J. Hickinbottom and D. R. Hogg, J. Chem. Soc. (1954), p. 4200.
11. S. N. Danilov in Symposium on "Reactions and methods of investigation of organic compounds" (Moscow, 1956), Vol. 4, p. 159.
12. K. Krasuskii, Zhur. Russ. Fiz. Khim. Obshch. 34, 556 (1902); A. E. Favorskii, Zhur. Russ. Fiz. Khim. Obshch. 38, 741 (1906).
13. D. Swern, G. N. Billen, and H. B. Knight, J. Am. Chem. Soc. 71, 1152 (1949).
14. O. A. Reutov, Theoretical Problems of Organic Chemistry [in Russian] (Izd. MGU, 1956), p. 293.
15. Y. Amiel, A. Löffler, and D. Ginsburg, J. Am. Chem. Soc. 76, 3625 (1954).
16. K. Mislow and A. K. Lazarus, J. Am. Chem. Soc. 77, 6383 (1955).
17. W. E. Bachmann, G. I. Fujimoto, and L. B. Wick, J. Am. Chem. Soc. 72, 1995 (1950).
18. A. F. Platé and A. A. Mel'nikov, Zhur. Obshch. Khim. 29, 1064 (1959).*
19. R. T. Arnold, J. S. Buckley, Jr., and R. M. Dodson, J. Am. Chem. Soc. 72, 3153 (1950).
20. P. Bruylants, Bull. soc. chim. Belg. 32, 307 (1923).
21. L. F. Fieser and J. Szmuszkovicz, J. Am. Chem. Soc. 70, 3352 (1948).
22. M. A. Haller, Bull. Soc. Chim. 31, 1073 (1922).
23. R. R. Dreisbach, Pressure-Volume-Temperature Relationships of Organic Compounds (1952).

* Original Russian pagination. See C. B. translation.

OXIDATION OF OLEFINS BY PERFORMIC ACID

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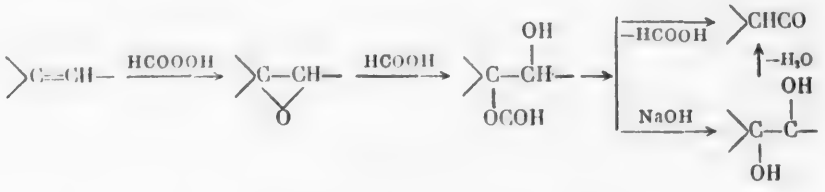
In one of the preceding communications [1] the preparation of 2-ethyl-, 2-n-propyl- and 2-n-butyl-1-cyclopentanones was described in illustration of a new method of single-step preparation of 2-alkyl-1-cyclopentanones by oxidation of 1-alkyl-1-cyclopentenes with performic acid.

In the present work, this method was applied to the preparation of other unsymmetrical ketones. Single-step oxidation with performic acid of 3-ethyl-2-pentene and of ethylidene-, n-propylidene- and n-butylidenecyclopentanes gave 3-ethyl-2-pentanone and methyl-, ethyl and n-propylcyclopentyl ketones in yields of 65.2, 52.7, 50.2, and 48.8 %, respectively.



Ketones can be obtained both after separation of intermediate products (except α-oxides) and without their separation, in a single step. 3-Ethyl-2-pentene and ethylidenecyclopentane were oxidized by performic acid, and then the formic acid and water were distilled off at reduced pressure to enable separation of the monoformates of the glycols. Yields of monoformates of 3-ethyl-2,3-pentanediol and of 1-(1-ethylol)-1-cyclopentanol were 44.6 and 46%, respectively. Hydrolysis of the monoformates gave 3-ethyl-2,3-pentanediol and 1-(1-ethylol)-1-cyclopentanol. Dehydration of these with 85% formic acid led to formation of 3-ethyl-2-pentanone and methylcyclopentyl ketone respectively in yields of up to 70%. All the prepared ketones were characterized as the semicarbazones and 2,4-dinitrophenylhydrazones. The constants of the ketones and of their derivatives are set forth in Table 1, and those of the glycols and their monoformates in Table 2.

The previously proposed single-step synthesis of ketones can accordingly be employed preparatively not only for the synthesis of 2-alkyl-1-cyclopentanones but also for synthesis of unsymmetrical aliphatic ketones with a branched carbon chain, alkylcyclopentyl ketones, etc. An advantage of this method is that no difficulties are involved in oxidation of the unsaturated hydrocarbons and in isolation of the ketones which are obtained in a sufficiently pure form and in good yields. The only serious difficulty might be the preparation of the starting unsaturated hydrocarbons.

EXPERIMENTAL

3-Ethyl-2-pentene was prepared by the method of [2] and had the following properties:

B. p. 94.9° (744 mm), $n^{20}D$ 1.4149, d^{20}_4 0.7206, MR_D 34.11; calc. 34.06.

TABLE 1

Ketones	Moles of hydrocarbon oxidized	Yield of ketone (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Melting point of semicarbazones	Melting point of 2,4-dinitrophenylhydrazones	Analysis of 2,4-dinitrophenylhydrazones found (%) C	H	N	calc. (%) C	H	N
3-Ethyl-2-pentanone (a)	0.3	65.2	136° (734)	1.4092	0.8230	34.31	34.54	134.5—135.5°	80—81° *	53.7	6.56	19.43, 19.12	53.05	6.17	19.04
Methylcyclopentyl ketone (b)	0.48	52.7	54—55.3 (20)	1.4436	0.9175	32.45	32.34	144.5—145.5	130—131	53.54, 53.51	6.12, 6.14	19.24, 19.43	53.42	5.52	19.17
Ethylcyclopentyl ketone (c)	0.25	50.2	77.5—78.5 (30)	1.4498	0.9176	36.94	36.95	139—140	143—144 *	54.60, 54.75	5.80, 5.87	18.63, 18.77	54.89	5.92	18.29
n-Propylcyclopentyl ketone (d)	0.25	48.8	90 -91.5 (25)	1.4488	0.9082	41.39	41.57	121—122	77.4—78 *	55.81, 55.73	6.25, 6.23	17.62, 17.46	56.24	6.29	17.49

Notes. Literature data: a) b. p. 136-137° (745 mm); $n^{20}D$ 1.4073 [4], d^{16} 0.825 [5]; semicarbazone m. p. 133-134° [6]; 97° [5]; b) b. p. 94.8-95° (99 mm), $n^{25}D$ 1.4411; d^{25}_4 0.9125 [7]; $n^{20}D$ 1.4440, d^{20}_{20} 0.9180 [8]; semicarbazone m. p. 144-145° [8]; 2,4-dinitrophenylhydrazone m. p. 126.9-127.3° [7]; c) b. p. 174-175°, $n^{16}D$ 1.4506, d^{16}_4 0.9177; semicarbazone m. p. 134° [9]; d) b. p. 198-199°, $n^{20}D$ 1.4486, d^{20}_4 0.9085; semicarbazone m. p. 123-124° [10], 110-111° [11].
Melting points of the derivatives of the ketones were determined as in [1].
* 2,4-Dinitrophenylhydrazones not described in the literature.

TABLE 2

Compound	Obtained (in mole)	Yield %	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	H	Calc. (%) C	H
3-Ethyl-2,3-pentanediol monoformate	0.22	44.6	71° (3)	1.4452	1.0051	42.44	42.32	59.50, 59.49	10.22, 10.27	59.97	10.07
1-(1-Ethylol)-1-cyclopentanol monoformate*	0.12	46.0	79 (2)	1.4725	1.0641	41.66	40.12	—	—	—	—
3-Ethyl-2,3-pentanediol**	0.13	95.1	73 (4, 5), 67 (3)	1.4525	0.9647	37.00	37.58	63.59, 63.11	12.22, 12.21	63.59	12.20
1-(1-Ethylol)-1-cyclopentanol	0.055	93.8	78—78.5 (2)	1.4799	1.0554	35.03	35.38	64.69, 64.71	10.80, 10.95	64.58	10.84

* Preparation could not be freed of trace of the corresponding glycol.
** Literature data: b. p. 105° (17 mm) [12]; 194-197°, d^{20} 0.957 [13].

We have already described [3] the starting substances for oxidation – ethylidene-, n-propylidene- and n-butylidenecyclopentanes.

Oxidation of hydrocarbons with performic acid. 3-Ethyl-2-pentene, ethylidene-, n-propylidene- and n-butylidenecyclopentanes were oxidized with a mixture of 85% formic acid and 30% hydrogen peroxide by the same procedure as for oxidation of 1-alkyl-1-cyclopentenes.

The ketones – 3-ethyl-2-pentanone, methyl-, ethyl- and n-propylcyclopentyl ketones – were obtained in a single step by distilling off the formic acid and water at atmospheric pressure from the products of oxidation of the respective unsaturated hydrocarbons [1] (Table 1).

The monoformates of 3-ethyl-2,3-pentanediol and 1-(1-ethylol)-1-cyclopentanol were obtained by distilling off the formic acid and water from the products of oxidation of the corresponding unsaturated hydrocarbons at a residual pressure of 40-45 mm. They were then saponified to the glycols (Table 2).

Dehydration of the glycols. Dehydration of 3-ethyl-2,3-pentanediol and 1-(1-ethylol)-1-cyclopentanol by boiling with 85% formic acid gave 3-ethyl-2-pentanone and methylcyclopentyl ketone respectively in a yield of up to 70%.

SUMMARY

The oxidation of 3-ethyl-2-pentene and of ethylidene-, n-propylidene- and n-butylidenecyclopentanes with performic acid was studied. This method led in a single step to 3-ethyl-2-pentanone, methyl-, ethyl- and n-propylcyclopentyl ketones in yields of 49-65%; also to 3-ethyl-2,3-pentanediol and 1-(1-ethylol)-1-cyclopentanol and their monoformates. Dehydration of these glycols does not involve a change in the carbon framework, and the corresponding ketones are formed.

LITERATURE CITED

1. A. F. Platé and A. A. Mel'nikov, Zhur. Obshch. Khim. 30, 1250 (1960).*
2. A. L. Liberman, T. V. Lapshina, and B. A. Kazanskii, Zhur. Obshch. Khim. 26, 46 (1956).*
3. A. F. Platé and A. A. Mel'nikov, Zhur. Obshch. Khim. 29, 1064 (1929).*
4. H. J. Lucas, J. Am. Chem. Soc. 51, 248 (1929).
5. J. Colonge, Bull. Soc. Chim. 41, 325 (1927).
6. J. Levy, Bull. Soc. Chim. 33, 1655 (1923).
7. R. P. Mariella and R. R. Raube, J. Am. Chem. Soc. 74, 518 (1952).
8. É. D. Venus-Danilova, Zhur. Obshch. Khim. 6, 697 (1936).
9. G. Vavon and V. M. Mitchovich, Bull. Soc. Chim. 45, 961 (1929).
10. I. N. Nazarov and M. S. Burmistrova, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1947), p. 51.
11. M. Mousseron, et al., Bull. Soc. Chim. (1946), p. 610.
12. D. Gauthier, Compt. rend. 152, 1101 (1911).
13. Tiffeneau and Dorlencourt, Compt. rend. 143, 126 (1906).

* Original Russian pagination. See C. B. translation.

DERIVATIVES OF β-DICARBONYL COMPOUNDS

II. SYNTHESIS OF 2,4-SUBSTITUTED PYRIMIDINES

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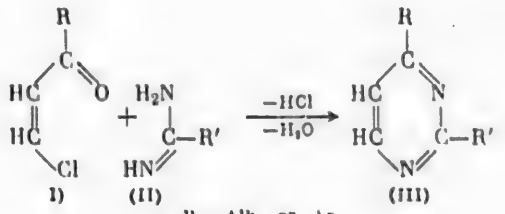
In this communication we consider the possibility of using β-chlorovinyl ketones and some of their transformation products for synthesis of compounds of the pyrimidine series containing a free or substituted amino group in the 2 position and an alkyl or aryl radical in the 4 position of the pyrimidine ring [1].

Pyrimidinic derivatives of this type were previously obtained by condensation of guanidine compounds with sodium salts of formyl ketones [2] or acylacetic esters [3]; in the latter case additional steps were needed – transformation of the resulting 4-hydroxypyrimidines into the corresponding 4-chloropyrimidines followed by dehalogenation [4]. β-Chlorovinyl ketones have recently become readily accessible substances; these are functional derivatives of the enolic forms of β-formyl ketones and are obtained by reaction of acid halides with acetylene [5] or vinyl chloride [6] in presence of Friedel – Crafts catalysts. The greater reactivity of β-chlorovinyl ketones enables them to be widely used for synthesis of various types of aliphatic, alicyclic and heterocyclic compounds [7].

We have shown that β-chlorovinyl ketones (I) can be successfully used for the synthesis of a cyclic pyrimidinic system (see [1]). Reaction of these compounds with guanidine (II, a) in presence of hydrogen chloride-binding agents or in a medium of concentrated sulfuric acid gave 4-substituted 2-aminopyrimidines (III, a). Similar reactions take place between β-chlorovinyl ketones and N-substituted guanidines [for example N-phenylguanidine (II, c) or N-sulfanylguanidine (II, d)] and benzamidine (II, b); in the latter case 4-substituted 2-phenylpyrimidines (III, b) are formed.



(I) (II) (III)

R = Alk or Ar
a) R′ = NH2,
b) R′ = C6H5,
c) R′ = NHC6H5,
d) R′ = NHSO2C6H4NH2-p.

We established subsequently that some derivatives of β-chlorovinyl ketones, for example β-dialkylaminovinyl ketones (IV, a) [8], trialkylketoalkenylammonium salts (IV, b) [9] or β-alkoxyvinyl ketones (IV, c) [10], can be used for preparation of pyrimidinic compounds of the type of interest to us (the reaction with guanidine was investigated). In all cases, interaction probably proceeds via the step of nucleophilic substitution of dialkyl-

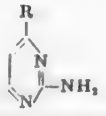
amino, trialkylammonium or alkoxy groups in the vinyl position, activated by conjugation with the carbonyl group.* Similar reactions occur with acetals of α-formyl ketones $RCOCH_2CH(OAlk)_2$ (V); this reaction may proceed through intermediate formation of β-alkoxyvinyl ketones (IV, c).

$$RCOCH=CHX.$$

(IV) a) $X = N(Alk)_2$,
b) $X = \overset{+}{N}(Alk)_2Cl^-$,
c) $X = OAlk$.

Typical conditions of preparation of the four types of pyrimidinic compounds with the help of various β-ketovinyl derivatives are specified in the experimental part. Yields and properties of the compounds prepared are set forth in Tables 1-4.

TABLE 1

4-Substituted 2-Aminopyrimidines 

R	Empirical formula	Method of preparation*	Yield %	Melting point: our data	Melting point: literature data
CH_3	$C_5H_7N_3$	(A) 56.0; (B) 55.0; (C) 80.3; (D) 64.0; (F) 82.5		158—159°	159—160° [4]
C_2H_5	$C_6H_9N_3$	(A)	64.5	136	140—141 [2, 14]
n-C_3H_7	$C_7H_{11}N_3$	(A)	86.9	122—123	122—123 [2]
iso-C_4H_9	$C_8H_{13}N_3$	(A) 71.0; (C) 66.2		118—119	119 [15]
n.-C_5H_{11}	$C_9H_{15}N_3$	(A)	60.6	89—90	90 [15]
C_6H_5	$C_{10}H_9N_3$	(A) 60.0; (D) 23.3		160—161	165 [2]
p-$O_2NC_6H_4$	$C_{10}H_8O_2N_4$	(A)	63.0	170—171 **	
o-BrC_6H_4	$C_{10}H_8N_3Br$	(E)	89.2	163—164 ***	
p-$CH_3OC_6H_4$	$C_{11}H_{11}ON_3$	(A)	59.7	189—190	185—187 [2]

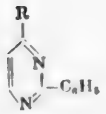
* Methods of preparation (see Experimental): (A) interaction of β-chlorovinyl ketones with guanidine in sulfuric acid; (B) the same in an alkaline medium; (C) from acetals of acylacetaldehydes; (D) from quaternary (β-acylvinyl)-ammonium salts; (E) from β-acylvinyl ethers; (F) from methyl-β-diethylaminovinyl ketone.

** Found %: N 25.92, 25.68. Calculated %: N 25.92.

*** Found %: N 16.94, 16.73; Br 32.52, 32.42. Calculated %: N 16.80; Br 32.00.

* Other cases of nucleophilic substitution of group X in compounds of type (IV) have been reported in the literature, for example the interaction of β-dialkylaminovinyl ketones (IV, a) with hydroxylamine [8] and the preparation of β-cyanovinyl ketones [11] or of products of ketovinylation of ethoxymagnesiummalonic ester [12] with the help of quaternary trialkyl-β-ketoalkenylammonium salts (IV, b). The employment of compounds of the type of (IV) and (V) for synthesis of pyrimidines unsubstituted in the 2 position has been described [13]; in this case, however, very much more drastic conditions were needed (prolonged heating with formamide at 180°).

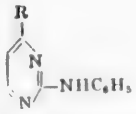
TABLE 2

4-Substituted 2-Phenylpyrimidines 

R	Empirical formula	Yield %	Temperature of melting	Temperature of boiling (pressure in mm)	d_4^{20}	n_D^{20}	% N our data	% N literature data
CH_3	$C_{11}H_{10}N_2$	62	25° *	275—279° (760)				
C_2H_5	$C_{12}H_{12}N_2$	35.2		135—140 (5)	1.0803	1.5840	15.08, 15.06	15.21
n-C_3H_7	$C_{13}H_{14}N_2$	40.6		153—155 (10)	1.0501	1.5795	14.04, 14.18	14.14
C_6H_5	$C_{16}H_{12}N_2$	53.6	71—72 **	197—198 (5)			12.13, 12.22	12.05

* Nitrate, m. p. 113°. Literature data [16]: base, m. p. 22.5°; nitrate m. p. 113°.
** Literature data [17]; m. p. 58-59°, b. p. 190-194° (3 mm).

TABLE 3

4-Substituted 2-Aminophenylpyrimidines 

R	Empirical formula	Method of preparation	Yield (%)	Temperature melting point	Temperature boiling point (pressure in mm)	% N found	% N calc.
CH_3	$C_{11}H_{11}N_3$	(A)	54.0	92—93° **		22.83, 22.86	22.70
C_2H_5	$C_{12}H_{13}N_3$	(A)	42.2	55—56	165° (5)	21.17, 21.17	21.10
n-C_3H_7	$C_{13}H_{15}N_3$	(A)	53.7	54—55	177 (8)	19.22, 19.86	19.71
iso-C_4H_9	$C_{14}H_{17}N_3$	(B)	74.8	49—50		18.55, 18.45	18.50
n-C_5H_{11}	$C_{15}H_{19}N_3 \cdot HNO_3$***	(B)	70.2			18.39, 18.38	18.42
C_6H_5	$C_{16}H_{13}N_3$	(B)	72.8	137—138		16.63, 16.74	16.97

* Method of preparation (see Experimental): (A) by reaction of β-chlorovinyl ketones with N-phenylguanidine; (B) from acetals of acylacetaldehydes.
** Literature data [18]: m. p. 92-93°.
*** Isolated as the nitrate.

EXPERIMENTAL

4-Substituted 2-Aminopyrimidines (Table 1)*

A) Reaction of β-chlorovinyl ketones with guanidine in sulfuric acid. 2-Amino-4-n-amylpyrimidine. To 30 ml of H_2SO_4 (d 1.84) was gradually added (with cooling and stirring) 6 g of guanidine sulfate, and then

* Melting points given in the text and tables are corrected.

TABLE 4

4-Substituted 2-Sulfanilaminopyrimidines

R	Empirical formula	Yield (%)	Melting point	
			our data*	literature data
CH_3	$C_{11}H_{12}O_2N_4S$	50.0	231—232°	231—232° [10]
C_2H_5	$C_{12}H_{14}O_2N_4S$	37.0	240—241	242 [15]
n-C_3H_7	$C_{13}H_{16}O_2N_4S$	51.5	216—217	217—218 [20]
iso-C_3H_9	$C_{14}H_{18}O_2N_4S$	32.2	227—228	232 [15]
n-C_5H_{11}	$C_{15}H_{20}O_2N_4S$	29.4	225—226	226 [15]
C_6H_5	$C_{16}H_{14}O_2N_4S$	23.0	261—262	264 [15]

* The capillary was inserted in an apparatus whose temperature was 30° below the melting point of the substance.

8 g of n-amyl-β-chlorovinyl ketone [6] was added at 15-20°. The reaction mixture was heated for 2 hours with gradual rise of temperature to 90-95°; HCl started to come off at 40°. The cooled reaction mixture was poured onto ice, the solution was neutralized with chalk, the precipitated $CaSO_4$ was filtered off, and the filtrate was acidified with HCl and concentrated in vacuo to a volume of 100 ml. To the residue was added solid NaOH; a precipitate came down. Yield 5 g (60.6 %); m. p. 89-90° (from 30% alcohol).

B) By the action of β-chlorovinyl ketones on guanidine nitrate in an alkaline medium. 2-Amino-4-methylpyrimidine. To a solution of 8.4 g of NaOH in 50 ml of methanol was added (with stirring) 13.4 g of guanidine nitrate; thereupon in the course of 1.5 hours 10.4 g of methyl-β-chlorovinyl ketone was introduced at 10-15°. The mixture was stirred for 5 hours on a boiling water bath. After the methanol had been distilled off, the residue (heated) was extracted with chloroform and the solvent was evaporated. Yield 6 g (55%); m. p. 158-159° (from alcohol).

C) From acetals of acylacetaldehydes. 2-Amino-4-isobutylpyrimidine. To a solution of 7.2 g of KOH in 90 ml of dry alcohol was added (with cooling) 17 g of isobutyl-β-chlorovinyl ketone [6]. After 24 hours, the precipitated KCl was filtered off, the alcohol was driven off, and the residue distilled in vacuo to give 14.6 g (62.1%) of isovaleroylacetaldehyde diethylacetal (see [10]).

B. p. 92° (7 mm), $n^{20}D$ 1.4520, d^{20}_4 0.9204, MR_D 56.19; calc. 56.29.

A mixture of 10.1 g of acetal and 4.5 g of guanidine carbonate was heated for 4 hours on a boiling water bath. After cooling, the mixture was dissolved in chloroform and filtered. Removal of the chloroform left 5 g (66.2%) of product; m. p. 118-119° (from aqueous alcohol).

D) From quaternary (β-acylvinyl)-ammonium salts. 2-Amino-4-phenylpyrimidine. A mixture of 2.6 g of N-(β-benzoylvinyl)-pyridinium chloride [9], 0.9 g of guanidine carbonate and 50 ml of methanol was heated for 6 hours on a boiling water bath; the methanol was taken off in vacuo, the residue was dissolved in 10% HCl, the acetophenone resulting from secondary reactions was extracted with ether, and the aqueous solution was made alkaline and extracted with chloroform. Yield 0.4 g (23.3%); m. p. 160-161°.

E) From β-acylvinyl ethers. 2-Amino-4-(o-bromophenyl)-pyrimidine. A solution of 12 g of o-bromophenyl-β-chlorovinyl ketone [6] in 25 ml of ethanol was stirred dropwise into a cooled solution of 3 g of KOH in 50 ml of dry ethanol. After 12-hours' standing, the precipitated KCl was filtered off, the alcohol was distilled off, and the residue was fractionated in vacuo. Yield of β-(o-bromobenzoyl)-vinylethyl ether 10 g (80.6 %).

B. p. 150-153° (3 mm), d^{20}_4 1.4110, $n^{20}D$ 1.5612, MR_D 58.56; calc. 58.35.

Found %: Br 32.50, 32.60. $C_{11}H_{11}O_2Br$. Calculated %: Br 32.12.

A mixture of 3.01 g of β-(o-bromobenzoyl)-vinylethyl ether, 0.9 g of guanidine carbonate and 10 ml of methanol was refluxed for 4 hours. The precipitate formed on cooling was filtered, the filtrate was evaporated in vacuo, the residue was dissolved in HCl, the solution was filtered in presence of carbon and made alkaline with ammonia. Yield of crystals 1.9 g (89.2%), m. p. 163-164° (from alcohol).

F) From β-dialkylaminovinyl ketones. 2-Amino-4-methylpyrimidine. To a solution of 0.46 g of metallic sodium in 100 ml of dry alcohol was added 1.9 g of guanidine hydrochloride followed by 2.8 g of methyl-β-diethylaminovinyl ketone. The mixture was stirred for 16 hours on a boiling water bath. The precipitated NaCl was filtered after cooling, and the alcohol was taken off in vacuo. Yield 1.8 g (82.5%); m. p. 157.5-158.5° (from water).

4-Substituted 2-Phenylpyrimidines (Table 2)

2-Phenyl-4-methylpyrimidine. Into a solution of 7 g of NaOH in 50 ml of methanol (cooled to 0°) was stirred gradually 9 g of benzamidine hydrochloride, followed at the same temperature (dropwise) by 6 g of methyl-β-chlorovinyl ketone. The mixture was boiled for 5 hours, cooled and filtered from NaCl; the methanol was taken off and the residue distilled to give 5 g (62%) of product; m. p. 25°; b. p. 275-279°.

4-Substituted 2-Phenylaminopyrimidines (Table 3)

A) By interaction of β-chlorovinyl ketones with N-phenylguanidine. 2-Phenylamino-4-methylpyrimidine. N-Phenylguanidine carbonate (8 g) was slowly stirred into 25 ml of 96% H_2SO_4 at 0-5°. Dropwise addition was then made, at 15-20°, of 5.2 g of methyl-β-chlorovinyl ketone. The mixture was heated for 2 hours at 90-95°, cooled and poured onto ice. Ammonia solution was then added until the mixture was alkaline. Yield 5 g (54%); m. p. 92-93° (from 30% ethanol).

B) From acetals of acylacetaldehydes. 2-Phenylamino-4-isobutylpyrimidine. A mixture of 2.02 g of isovaleroylacetaldehyde diethylacetal and 1.66 g of N-phenylguanidine carbonate was heated for 4 hours at 160°. After cooling, the mixture was poured onto ice and HNO_3 solution (1:4) was added until the pH was 3. The precipitated nitrate was treated with NaOH solution, washed with water and dried. Yield 1.7 g (74.8%); m. p. 49-50°.

4-Substituted 2-Sulfanilamidopyrimidines (Table 4)

2-Sulfanilamido-4-methylpyrimidine. To a solution of 120 g of NaOH in 1500 ml of methanol was added 214 g of sulfanylguanidine. Afterward 104.5 g of methyl-β-chlorovinyl ketone was added gradually at 50-60°. The mixture was stirred for 5 hours at the boiling point of methanol. After cooling, the precipitate was filtered off, dissolved in 1500 ml of hot water, filtered in presence of carbon, and treated with 10% HCl (to pH 7). Yield 132 g (50% calculated on the β-chlorovinyl ketone); m. p. 231-232°. Unreacted sulfanylguanidine was recovered (90 g) after evaporation of the methanol.

SUMMARY

1. Reaction of β-chlorovinyl ketones with guanidine, N-phenylguanidine, sulfanylguanidine or benzamidine is a convenient route to pyrimidinic compounds substituted in the 2 and 4 positions.

2. In these reactions the place of β-chlorovinyl ketones can be taken by acetals of acylacetaldehydes, β-dialkylaminovinyl ketones, quaternary β-acylvinylammonium salts or β-acylvinyl ethers.

LITERATURE CITED

1. V. T. Klimko, V. A. Mikhalev, and A. P. Skoldinov, Author's Certificates Nos. 75,978 (1949) and 91,299 (1951).
2. E. Benary, Ber. 63, 2601 (1930).
3. J. Jäger, Lieb. Ann. 262, 365 (1891).
4. S. Gabriel and J. Colman, Ber. 36, 3379 (1903); 32, 2924 (1899).
5. A. N. Nesmeyanov, N. K. Kochetkov, and M. I. Rybinskaya, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1950), p. 350.

6. V. T. Klimko, V. A. Mikhalev, and A. P. Skoldinov, Author's Certificate No. 89,803 (1950); Zhur. Obshch. Khim. 27, 370 (1957).*
7. N. K. Kochetkov, Uspekhi Khim. 24, 32 (1955).
8. N. K. Kochetkov, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1953), p. 991;* (1954), p. 55.*
9. V. T. Klimko, A. Ya. Khorlin, V. A. Mikhalev, A. P. Skoldinov, and N. K. Kochetkov, Author's Certificate No. 103,767 (1956); Zhur. Obshch. Khim. 27, 62 (1957).*
10. A. N. Nesmeyanov, N. K. Kochetkov, and M. I. Rybinskaya, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1951), p. 395.
11. A. N. Nesmeyanov and M. I. Rybinskaya, Doklady Akad. Nauk SSSR 115, 315 (1957).*
12. N. K. Kochetkov and L. I. Kudryashov, Zhur. Obshch. Khim. 28, 1967 (1958).*
13. H. Bredereck, R. Gompper, and G. Morlock, Ber. 90, 942 (1957).
14. W. Caldwell and W. Ziegler, J. Am. Chem. Soc. 58, 287 (1936).
15. G. Raiziss and M. Freifelder, J. Am. Chem. Soc. 64, 2340 (1942).
16. J. Schmidt, Ber. 35, 1575 (1902).
17. U. S. Patent 2,524,479; Chem. Abs. 45, 1168 (1951).
18. U. S. Patent 2,570,087; Chem. Abs. 46, 5093 (1952).
19. R. Roblin, J. Williams, and P. Winnek, J. Am. Chem. Soc. 62, 2002 (1940).
20. J. Sprague, L. Kissinger, and R. Lincoln, J. Am. Chem. Soc. 63, 3028 (1941).

* Original Russian pagination. See C. B. translation.

MASS-SPECTROSCOPIC INVESTIGATION OF SOME HOMOLOGS OF TETRAHYDROTHIOPHENE

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Mass-spectroscopic investigation of homologous series of various compounds is of interest both as a means of clarifying the analytical possibilities of the method and for establishing the special features of interaction of molecules with electrons. The values so obtained are unique molecular constants. According to modern ideas about the mechanism of dissociative ionization, mass spectra are directly associated with molecular structure. The first step in the process is the loss of an electron from the molecule (formation of a molecular ion); the second is the breakdown of the molecular ion which proceeds in several directions simultaneously. The predominating processes are those requiring the least expenditure of energy, and the distribution of ionic intensities in mass spectra is determined mainly by the magnitude of the bond energy in the molecule. The presence in a molecule of groupings stable to electron bombardment or of weakened bonds between atoms leads to formation of fragment ions and to the appearance of characteristic peaks in the spectrum. Extensive investigations of the mass spectra of homologous series of various organic compounds [1] have enabled the fundamental relations between mass spectra and molecular structure to be established and opened the way to utilization of the mass-spectrometric method for the qualitative identification and quantitative analysis of the compounds concerned.

Relatively little work has appeared on the mass spectra of sulfur compounds; only the thiophene series has been closely studied. As would be expected, the spectral characteristics of thiophenes are similar in many respects to those of alkylbenzenes [2].

In this paper we submit the results of a mass-spectroscopic investigation of a homologous series of α-alkyltetrahydrothiophenes containing radicals of normal structure with chain lengths of C_1 to C_6.

The MS-1 instrument was used in the work. We previously [3] described a modification of this instrument for use in analysis of hydrocarbon gases. A number of fresh problems arose when the mass-spectroscopic technique was extended to the examination of compounds of higher molecular weight (above 80) as well as of substances with high adsorptivity. These problems include primarily the introduction of liquid samples into the admission system, adsorption on the walls of the apparatus and the influence of the temperature of the ion source on the constancy of intensity distribution in the spectra. Adsorptive phenomena gave rise to "memory" of the apparatus with consequent distortion of the spectra and analytical errors. Memory was eliminated and the stability of measurements was improved with the help of a heating system for the inlet. The ion source and the analyzer of the mass spectrometer were also thermostated.

The charging system comprised: a) A four-liter vessel to ensure constant pressure of the sample during investigation; b) diaphragms with 10-20 μ openings through which the gas was admitted to the ion source in a molecular stream; c) diffusion and mechanical pumps; d) test-tubes for introduction of samples with ground-glass connections; e) metal shut-off valves. The optimum working temperature was established by investigation of the temperature dependence of the intensities of the analytical peaks in the spectra of various mixtures. It was found that maximum stability and reproducibility of the mass-spectrometric measurements was attained at 125-150°.

The mass spectra of α-alkyltetrahydrothiophenes were investigated under the following working conditions: accelerating voltage 2500 v, emission current 1.5 ma, electron ionization energy 70 v, temperature of the inflow system of the ion source and analyzer 125 ± 1°.

The mass spectra were analyzed by changing the voltage of the magnetic field with the help of a specially constructed device ensuring smooth spectral tracing in the range of masses up to 300.

Mass spectra of α-methyl-, α-ethyl-, α-propyl-, α-butyl-, α-amyl- and α-hexyltetrahydrothiophenes were plotted. The mass spectra of tetrahydrothiophene and α-methyltetrahydrothiophene have already been published in the American Petroleum Institute's catalog of mass spectra; those of the remaining homologs were here obtained for the first time. The distribution of intensities in the spectra of tetrahydrothiophene derivatives is set forth in Table 1. The intensities of the ionic currents are expressed as percentages of the highest peak in the spectra.

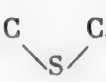
TABLE 1

Distribution of Intensities in Mass Spectra of Tetrahydrothiophenes

Masses and possible composition of fragment ions	Tetrahydrothiophene	α-Methyltetrahydrothiophene (M 102)		α-Ethyltetrahydrothiophene (M 116)	α-n-Hexyltetrahydrothiophene (M 130)	α-n-Butyltetrahydrothiophene (M 144)	α-n-Amyltetrahydrothiophene (M 158)	α-n-Hexyltetrahydrothiophene (M 172)
	1*	1*	2**					
15 CH_3^+	3.0	—	11.6	—	3.7	4.2	6.5	0.6
26 $C_2H_2^+$	6.1	1.03	7.6	4.4	2.6	1.8	5.5	2.2
27 $C_2H_3^+$	24.0	17.43	30.0	26.9	21.6	18	24.6	16.3
39 $C_3H_3^+$	14.0	19.5	36.5	26.6	19.8	13.9	16.0	10.0
41 $C_3H_5^+$	10.0	33.7	41.8	33.3	25.0	23.6	35.4	22.5
42 $C_3H_6^+$	3.8	3.26	6.4	5.2	3.4	7.1	4.0	2.5
43 $C_3H_7^+$;rearrange.	1.9	0.896	2.9	2.1	2.0	2.7	10.6	6.8
45 CHS^+	36.8	32.5	38.6	34.2	23.7	17.3	13.2	10.1
46 CH_2S^+	31.9	8.96	11.1	8.5	3.8	2.2	1.4	1.0
47 rearrangement	26.0	11	10.6	10.4	9.2	6.1	5.2	4.3
53 $C_4H_5^+$	4.6	7.21	11.1	12.3	8.6	7.1	12.0	5.3
54 $C_4H_6^+$	13.0	1.75	2.1	3.9	3.7	2.2	3.4	2.6
55 $C_4H_7^+$	12.0	11.2	28.0	12.4	13.2	9.0	16.6	9.5
56 C_2S^+; $C_4H_8^+$	0.64	4.5	5.4	1.7	1.2	0.7	3.4	1.4
57 C_2HS^+; $C_4H_9^+$	2.74	1.77	1.9	0.8	0.3	0.5	6.3	1.5
58 $C_2H_2S^+$	8.22	6.31	9.8	6.9	4.3	2.5	1.4	1.5
59 $C_2H_3S^+$	17.6	20.4	26.8	17.0	11.7	8.7	6.0	4.9
60 C_2H_4S	100	19.2	18.5	9.3	5.2	4.1	4.5	2.9
61 rearrangement	4.12	7.52	6.9	5.7	3.1	2.2	3.4	1.8
67 $C_5H_7^+$	4.40	5.38	9.0	14.3	9.2	6.8	10.8	6.7
68 $C_5H_8^+$; C_3S^+	0.16	6.03	6.6	1.2	2.2	2.4	4.3	2.9
69 $C_5H_9^+$; C_3HS^+	0.58	3.49	3.6	3.1	1.1	1.5	7.1	3.7
71 $C_3SH_3^+$;	—	1.69	1.6	2.4	1.5	1.2	3.4	1.2
73 $C_3H_5S^+$	—	3.09	3.7	4.7	3.1	1.9	2.5	1.4
81 C_4HS^+	0.18	0.1	1.3	2.4	4.2	—	6.3	3.0
85 $C_4H_4S^+$; $C_6H_{13}^+$	2.82	3.01	5.0	6.7	5.9	4.9	4.5	3.1
87 $C_4H_7S^+$	15.9	100	100	100	100	100	100	100
88 $C_4H_8S^+$	53.5	5.0	4.5	6.1	5.5	5.6	5.5	5.9
101 $CH_2C_4H_7S^+$		4.21	3.7	15.0	16.3	10.2	22.0	4.8
102 $CH_3C_4H_7S^+$		42.4	42.3	1.7	0.6	0.15	—	0.5
115 $C_2H_4C_4H_7S^+$					0.6	0.7		0.8
116 $C_2H_5C_4H_7S^+$				28.5	0.6			0.1
129 $C_3H_6C_4H_7S^+$					0.3	0.1		5.6
130 $C_3H_7C_4H_7S^+$				3.51	18.3			0.5
143 $C_4H_8C_4H_7S^+$								0.6
144 $C_4H_9C_4H_7S^+$						14.0		0.1
158 $C_5H_{11}C_4H_7S^+$							12.78	
171 $C_6H_{12}C_4H_7S^+$								0.2
172 $C_6H_{13}C_4H_7S^+$								8.8

* American Petroleum Institute data.

** Data of Scientific Research Institute of the Petroleum Industry.

In the mass spectra of all of the α-alkyltetrahydrothiophenes investigated the highest peak is that of mass 87, corresponding to formation of the tetrahydrothiophene ion due to detachment of the alkyl radical. A considerable number of ions of the type of  are present in the mass spectra of tetrahydrothiophene and methyltetrahydrothiophene due to rupture of the tetrahydrothiophene ring; with increasing length of side-chain their relative number decreases, evidently in consequence of the stabilizing influence of the alkyl radical.

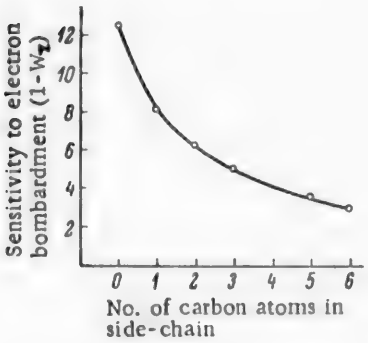


Fig. 1. Stability characteristics of α-alkyltetrahydrothiophenes.

Another noteworthy feature is the regular relative fall in intensity of the molecular ions with increasing molecular weight of the tetrahydrothiophenes (Fig. 1).

The resistance of the molecules to electron bombardment is expressed as the breakdown probability W_Z [4] and is calculated from the formula

$$(1 - W_Z) = \frac{\Sigma I_{frag}}{\Sigma (I_{frag} + I_{mol})},$$

where I_{frag} and I_{mol} are the intensities of fragment and molecular ions, respectively.

The fall in stability with increasing number of carbon atoms in the side chain, characterizing α-alkyltetrahydrothiophenes, is also observed with other classes of organic compounds. However, the curves can vary slightly in form depending on the structure.

The sensitivity of the investigated compounds was characterized by the ratios of the molecular and highest peaks in the spectrum of the investigated substance and of benzene. Values of the coefficients of relative sensitivity of molecular and maximum peaks are presented in Table 2. The observed regularities are depicted graphically in Fig. 2. The first member of the series (tetrahydrothiophene) has the lowest sensitivity of the molecular ion; introduction of a methyl radical considerably increases the relative sensitivity but the value declines linearly with increasing length of side-chain.

TABLE 2

Coefficients of Relative Sensitivity of Tetrahydrothiophene and α-Alkyltetrahydrothiophenes

Compound	Coefficients of Relative Sensitivity			
	of molecular ions		of highest peaks	
	1*	2**	1*	2**
Tetrahydrothiophene	–	0.185		0.345
α-Methyltetrahydrothiophene	0.318	0.254	0.73	0.61
α-Ethyltetrahydrothiophene	0.274	–	0.96	–
α-Propyltetrahydrothiophene	0.240	–	1.31	–
α-Butyltetrahydrothiophene	0.185	–	1.32	–
α-Amyltetrahydrothiophene	0.170	–	1.33	–
α-Hexyltetrahydrothiophene	0.105	–	1.30	–

* Data of All-Union Scientific Research Institute of the Petroleum Industry.

** American Petroleum Institute data.

The sensitivities of the highest peaks of the spectra change in a somewhat different manner: at first the sensitivity increases with increasing chain length and then reaches a nearly constant value. Extrapolation of the curve in the direction of zero number of carbon atoms in the side-chain gives a sensitivity for tetrahydrothiophene close to the literature value.

The total ionization of alkyltetrahydrothiophenes is directly related to the mass spectra and sensitivities of the compounds. Investigations on various types of hydrocarbons show that in a homologous series the total ionization increases linearly with the number of carbon and hydrogen atoms. The magnitude of total ionization of isomers sometimes enables calculation of all of the isomers as one group in analysis without identification of individual compounds [5]. Calculations show that the total ionization of α-alkyltetrahydrothiophenes is likewise directly proportional to the molecular weight and is constant per unit of molecular weight (Fig. 3). The calculated and experimental values of total ionization are in good agreement (curve 2 of Fig. 3). Since the total ionization is one of the most general mass-spectrometric characteristics (little dependent on instrumentation factors), it can be used for the structural-group analysis of heterocyclic compounds.

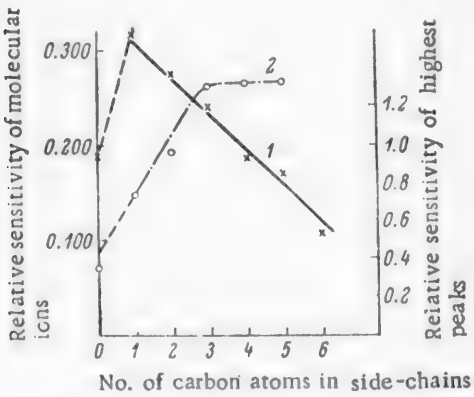


Fig. 2. Influence of length of side-chain in α-alkyltetrahydrothiophenes on the magnitude of the relative sensitivity of molecular and fragment ions. 1) Sensitivity of molecular ions; 2) sensitivity of fragment ions.

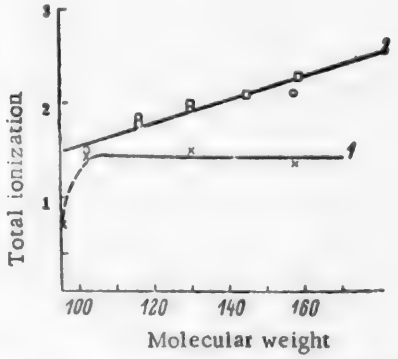


Fig. 3. Relation between total ionization of α-alkyltetrahydrothiophenes and molecular weight. 1) Total ionization related to molecular weight; 2) total ionization of α-alkyltetrahydrothiophenes. (Circles denote experimental values, rectangles denote values calculated from the formula).

Identification of α-alkyltetrahydrothiophenes in mixtures and their quantitative mass-spectrometric determination are effected on the basis of the highest peak in their mass spectra (m/e-87); this peak is usually not intersected by the spectra of other compounds. Individual compounds of this series in isolated cases can be determined from the peaks of the molecular ions, although such a determination is very much less sensitive. Determination of α-alkyltetrahydrothiophenes in mixtures are accurate to 10-15 rel. %.

SUMMARY

1. A mass-spectrometric investigation was made of the first members of the α-alkyltetrahydrothiophene series (C_1 to n-C_6 in the side-chain); the distribution of mass intensities in the spectra was established, the relative sensitivities were determined, the dependence of these values on molecular weight was examined, and the total ionization was calculated.

2. The possibility of structural identification and of qualitative analysis of mixtures of α-alkyltetrahydrothiophenes was demonstrated. Quantitative analyses of mixtures are accurate (judging by preliminary results) to within about 10-15 rel. %.

LITERATURE CITED

1. F. W. McLafferty, Anal. Chem. 28, 306 (1956).
2. I. W. Kinney and G. L. Cook, Anal. Chem. 24, 1391 (1952).
3. K. I. Zimina, A. A. Polyakova, M. V. Tikhomirov, and N. S. Sosina, Symposium: Composition and Properties of Petroleums and Gasoline-Kerosine Fractions [in Russian] (Izd. AN SSSR, 1957), p. 72.
4. M. Z. Pohl, Naturforsch. 96, 188 (1954).
5. G. F. Crable, and N. D. Goggeshall, Anal. Chem. 30, 311 (1958).

INVESTIGATION OF THE ISOXAZOLE SERIES

X. MERCURIZATION OF ISOXAZOLES

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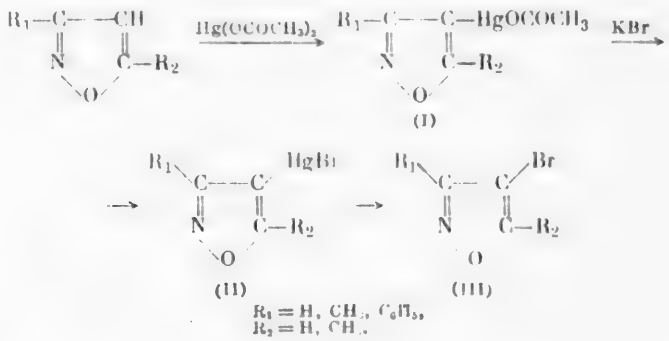
At present only a limited number of electrophilic substitution reactions are known for isoxazole (nitration, halogenation, sulfonation, chloromethylation), in which it is noted that whenever the 4-position in the ring is free, substitution takes place at that point [1, 2]. Substitution in the isoxazole ring is more difficult to carry out than in the benzene ring [2]. Considering the limited number of substitution reactions known for isoxazole, an increase in the range of such reactions is both of basic theoretical and of practical interest in the field of the chemistry of heterocyclic compounds. With this in view, we have studied the mercurization of isoxazole derivatives, which, as is known, proceeds in a rather unique manner for compounds of an aromatic nature. The sole example of mercurization of the isoxazole ring – mercurization of 5-phenylisoxazole – was recently described by us [1].

This reaction has been extended by us, and it has been shown that both alkylisoxazoles (3- and 5-methyl-, 3,5-dimethylisoxazoles) and arylisoxazoles (3-phenylisoxazole) can take part in a mercurization reaction. In each case, mercurization is carried out by heating the isoxazole compound with mercuric acetate in a solvent-free system on a water bath. Mercuric acetates (I), high yields of which are obtained in this manner, can be readily converted into mercuric bromides (II) by treatment with potassium bromide.



It should be noted that 3-phenylisoxazole is mercurized with somewhat greater difficulty than 5-phenylisoxazole [1], and 3-methylisoxazole with greater difficulty than 5-methylisoxazole. Mercurization of unsubstituted isoxazole could not be accomplished, since, on heating it with mercuric acetate, slow oxidation with formation of mercurous salts occurred. It is of interest that mercurization of isoxazoles is always achieved with somewhat greater ease than mercurization of benzene derivatives [3]. This fact shows once again the similarity of the isoxazole to the pyridine ring [2], which is known to be mercurized quite successfully, despite its considerable inertness to electrophilic substitution reactions [3]. Another difference between the mercurization of

isoxazoles and that of aromatic derivatives is the constant behavior of monosubstituted isoxazoles when isomer-formation is possible; in every case of mercurization, only a single substitution product is obtained. It should be emphasized that pyridine, unlike aromatic hydrocarbons, is mercurized in a similar well-defined manner [3].

To determine the structure of the mercuric derivatives obtained, we studied their conversion into the corresponding bromides (III) by treatment with bromine in dichloroethane. Bromides obtained from the mercuric derivatives of 3- and 5-methylisoxazoles had constants agreeing with those of 4-bromo- 3-methyl- and 4-bromo-5-methylisoxazoles, obtained previously by direct bromination. The bromide obtained by treatment of the mercuric derivative of 3-phenylisoxazole was identical with the substance obtained by direct bromination of 3-phenylisoxazole. Since bromination of the various isoxazole derivatives proceeds only in the 4-position, the bromide obtained must of necessity be considered 4-substituted, and consequently the mercuric derivative must be 3-phenylisoxazole-4-mercuric bromide (see, for example, [1, 2]).

EXPERIMENTAL

Mercurization of 3-phenylisoxazole. 8.55 g of 3-phenylisoxazole was heated on a water bath with 18.5 g of mercuric acetate until a transparent, oily substance was obtained. 23.6 g (99%) of 3-phenylisoxazole-4-mercuric acetate was obtained, no crystallization occurring on prolonged storage. The substance was dissolved in aqueous dioxane and a solution of 7 g of KBr in aqueous dioxane added. The precipitate deposited was filtered off and dried. Yield of 3-phenylisoxazole-4-mercuric bromide was 20 g (80%). M. p. 217-219° C (from water); colorless crystals.

Found %: C 25.62, 25.52; H 1.71, 1.77. $C_9H_6ONBrHg$. Calculated %: C 25.50; H 1.65.

12.2 g of 3-phenylisoxazole-4-mercuric bromide was dissolved in dichloroethane, 4.6 g of bromine added, and boiled until colorless. The solvent was distilled off and the residue extracted with ether. After distilling off the ether, 4.5 g (70%) of 4-bromo-3-phenylisoxazole was obtained, m. p. 48-49°. The substance did not give a m. p. depression with 4-bromo-3-phenylisoxazole, obtained by direct bromination of 3-phenylisoxazole.

Bromination of 3-phenylisoxazole. A mixture of 8 g of 3-phenylisoxazole, 9.4 g of bromine, and 0.1 g of powdered iron was heated at 110-130° for 6 hours until evolution of hydrogen bromide ceased. The reaction mixture was diluted with ether, the ethereal solution washed with $Na_2S_2O_3$ solution, water, and dried with $MgSO_4$. The ether was distilled off and the residue vacuum-distilled. 8.6 g of a substance with b. p. 127-130° (5 mm) was obtained, from which, on freezing, was then obtained 3 g of 4-bromo-3-phenylisoxazole, m. p. 45-47°. Yield relative to 3-phenylisoxazole used in the reaction was 80%. M. p. 50-51° (from petroleum ether).

Found %: C 48.18, 48.28; H 2.75, 2.77. C_9H_6ONBr. Calculated %: C 48.24; H 2.69.

Mercurization of 5-methylisoxazole. 0.5 g of 5-methylisoxazole was heated on a water bath with 1.9 g of mercuric acetate in a manner similar to that described above. 2 g (97%) of 5-methylisoxazole-4-mercuric acetate was obtained. Shining, colorless flakes, m. p. 124-124.5° (from water).

Found %: C 20.84, 20.81; H 2.12, 2.07. $C_6H_7O_3NHg$. Calculated %: C 21.08; H 2.05.

An aqueous solution of 15 g of 5-methylisoxazole-4-mercuric acetate was treated with a solution of 5.3 g of KBr. The mercuric bromide obtained was dissolved in dichloroethane and treated with the calculated quantity of bromine. Yield of 5-methyl-4-bromoisoxazole was 4.35 g (60%).

B. p. 147-148°, $n^{20}D$ 1.4915. Data in the literature [4]: b. p. 147-148°; $n^{22}D$ 1.4909.

Found %: Br 49.65, 49.87. C_4H_4ONBr. Calculated %: Br 49.38.

Mercurization of 3-methylisoxazole. The mercuric acetate of 3-methylisoxazole was obtained in a manner similar to that described for 5-phenylisoxazole from 4.9 g of 3-methylisoxazole and 18.7 g of mercuric acetate. Yield, 20 g (quantitative). M. p. 154-155° (from water).

Found %: C 20.93, 20.83; H 2.10, 2.09. $C_6H_7O_3NHg$. Calculated %: C 21.08; H 2.05.

10.2 g of the mercuric acetate obtained was dissolved by heating in water, and a solution of 3.6 g of KBr added. 8.5 g (80%) of 3-methylisoxazole-4-mercuric bromide was obtained, m. p. 151-154°. To a solution of

the mercuric bromide in dichloroethane was added a solution of 3.7 g of bromine in dichloroethane, the mixture then being boiled until colorless. The dichloroethane was distilled off, the residue filtered, and the filtrate distilled. 1.4 g of 4-bromo- 3-methylisoxazole was obtained. B. p. 143-145°, $n^{20}D$ 1.4742. Data in the literature [4]: b. p. 142.5-144.5°.

Mercurization of 3,5-dimethylisoxazole. The mercuric acetate of 3,5-dimethylisoxazole was obtained similarly by heating, in a water bath for 20 minutes, 3 g of 3,5-dimethylisoxazole with 9.8 g of mercuric acetate. Yield, 10 g. M. p. 104-105° (from water).

Found %: C 23.35, 23.41; H 2.40, 2.43. $C_7H_9O_5NHg$. Calculated %: C 23.66; H 2.53.

6.1 g of the mercuric acetate of 3,5-dimethylisoxazole was dissolved in water and 2.04 g of KBr, in aqueous solution, added. 6.3 g of 3,5-dimethylisoxazole-4-mercuric bromide was obtained in a similar manner, m. p. 171-172° (from water).

SUMMARY

1. Mercurization of 3-methyl-, 5-methyl-, 3,5-dimethyl-, and 3-phenylisoxazole was accomplished by heating them with mercuric acetate.

2. The composition of the mercuric derivatives obtained was determined by their conversion into the corresponding bromides. It was shown that mercurization always occurred in the 4-position of the isoxazole ring.

LITERATURE CITED

1. N. K. Kochetkov and E. D. Khomutova, Zhur. Obshch. Khim. 28, 359 (1958).°
2. N. K. Kochetkov and E. D. Khomutova, Zhur. Obshch. Khim. 29, 535 (1959).°
3. L. G. Makarova and A. N. Nesmeyanov, Synthetic Methods in the Field of Metalloorganic Mercury Compounds [in Russian] (Izd. AN SSSR, 1945), No. 34, p. 50.
4. A. Quilico and R. Justoni, Rend. ist Lombardo sci. 69, 587 (1936); Chem. Abs. 32, 7455 (1938).

° Original Russian pagination. See C. B. translation.

OXIDATION OF 4-NITROACENAPHTHENE TO NITRONAPHTHALIC ACID

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Oxidation of organic substances with sodium bichromate is usually carried out in the presence of acetic or sulfuric acids. Acetic acid acts as a solvent and also gives best results. Oxidation by sulfuric acid, on the other hand, is usually accompanied by combustion of part of the substance being oxidized and by tar or resin formation.

Replacement of these acids by hydrochloric has not been suggested so far. The cause of this is obviously the well-known oxidation of hydrogen chloride by bichromate, with evolution of chlorine. Meanwhile, as early as 1921, Kaminskii established [1] that addition of a small quantity of hydrochloric acid during oxidation of toluene by bichromate and sulfuric acid considerably accelerates the reaction and gives a better yield. V. Dzirkal used hydrochloric acid as an additive in the oxidation of the dithio-group by nitric acid [2].

We have established that it is possible to carry out oxidation (at least, of some organic substances) with bichromate in a hydrochloric acid medium without evolution of chlorine. For this to occur, the hydrochloric acid should not be used above a certain maximum concentration (varying with the particular compound undergoing oxidation) and should be used in a definite ratio to the quantity of bichromate employed in the reaction. In the present work this is exemplified by the oxidation of 4-nitroacenaphthene.

4-Nitronaphthalic acid was first obtained by Quncke [3] by heating acenaphthene with dilute nitric acid; from 30 g of acenaphthene he obtained 2 g of acid. Graebe and Brions obtained it by oxidation of 4-nitroacenaphthene with sodium bichromate in glacial acetic acid. The yield is not stated by the authors [4]. We studied the oxidation of 4-nitroacenaphthene in a sulfuric acid medium and found that the oxidation process proceeds slowly in the presence of sulfuric acid and gives low yields.

Oxidation of 4-nitroacenaphthene proceeds rapidly and smoothly in a hydrochloric acid medium, no resinification or combustion being observed. Yield of 4-nitronaphthalic acid obtained is 80-85%. The quantity of hydrochloric acid should not exceed 5 moles of hydrogen chloride per mole of bichromate, and hydrogen chloride concentration should not be higher than 20%. If not, oxidation of hydrogen chloride takes place with evolution of chlorine. Better results are obtained in the presence of a double proportion of bichromate and with vigorous stirring. In this work, using hydrochloric acid in amounts and in concentrations no greater than those indicated, the oxidation product obtained is completely chlorine-free (Beilstein test).

EXPERIMENTAL

Oxidation of 4-nitroacenaphthene. Into a flask fitted with reflux condenser and stirrer was introduced 10 g of nitroacenaphthene, bichromate and hydrochloric acid. The mixture was heated on a water bath, then cooled to room temperature, the precipitate filtered off, washed free of bichromate with water, and then treated with a 5% soda solution for 1 hour on a water bath. The soda solution was filtered from the undissolved residue and the filtrate acidified with hydrochloric acid. The precipitated 4-nitronaphthalic acid was filtered, washed with water, and dried at 100-110° C; at this temperature it was fully converted to the anhydride.

In other experiments, the oxidation product was not treated with soda solution, but was dried immediately, and its melting point determined. The oxidation product in this case usually melted at 200-212°. However, this product, reprecipitated from soda solution, usually had a m. p. of 216-222°. In the most successful experiments, oxidizing 10 g of nitroacenaphthene, we obtained 9.5-10 g of nitronaphthalic anhydride and 0.5-1.0 g of partially oxidized residue, which was not extracted by soda solution. The residues from several experiments were then reoxidized and gave a further amount of nitronaphthalic anhydride, the yield being 50-60% of the weight of the residues undergoing oxidation. A good yield was obtained only with 100% excess bichromate. The degree of stirring influenced the yield greatly. Other conditions being equal, poor agitation was found to lower the yield by 50%.

The influence of various factors on the yield of 4-nitronaphthalic anhydride is shown in Tables 1-4.

TABLE 1

Effect of Hydrochloric Acid Concentration on Rate of Oxidation of 10 g of Nitroacenaphthene over a Period of 150 Minutes

Expt. No.	Quantity of HCl (in ml)	Concentration of HCl (%)	Yield	
			nitronaphthalic anhydride	partially oxidized residue
1	150	20	8.7	1.9
2	170	18	9.4	1.3
3	180	17	9.45	1.55
4	195	16	9.0	1.95
5	200	15	8.9	1.75

TABLE 2

Effect of Quantity of HCl on Rate of Oxidation of 10 g of Nitroacenaphthene over a Period of 90 Minutes

Expt. No.	Quantity of HCl (in ml)	Concentration of HCl (%)	Moles of HCl per mole of bichromate	Yield	
				nitronaphthalic anhydride	residue
1	80	20	2.6	3.4	5.6
2	100	20	3.3	4.35	4.45
3	150	20	5	7.55	3.4
4	200	20	6.6	5.05	6.0
5	225	20	7.4	2.1	10.45

TABLE 3

Effect of Ratio Bichromate :Hydrochloric Acid (20% HCl)

Expt. No.	Quantity of $Na_2Cr_2O_7 \times 2H_2O$ (in g)	Quantity of HCl (in ml)	Duration of Expt. (hours)	Yield	
				nitronaphthalic anhydride	residue
1	30	60	2	3.0	5.8
2	40	120	2	7.85	2.45
3	50	150	2	8.8	2.05
4	50	170	4	9.9	0.8
5	50	210	4	9.55	0.5

TABLE 4

Effect of Heating Time on Yield of Nitronaphthalic Anhydride (10 g of Nitroacenaphthene and 170 ml of 18% HCl were taken)

Expt. No.	Heating time	Yield	
		nitronaphthalic anhydride	incompletely oxidized residue
1	1 hour	4.3	5.3
2	2 hour	9.0	1.8
3	2 hr 30 min	9.4	1.3
4	3 hour	10.0	0.9
5	4 hour	9.8	0.8

SUMMARY

It has been shown that oxidation of nitroacenaphthene can be achieved using bichromate in a hydrochloric acid medium and that a chlorine-free oxidation product can be obtained. A method of obtaining 4-nitronaphthalic anhydride in 80-85% yield has been developed.

LITERATURE CITED

1. P. Kaminskii, Zhurn. Farmats. Inst., 2 (1921).
2. V. Dzirkal, Collection of the IREA* [in Russian] (GONTI, Leningrad-Moscow, 1938), p. 318.
3. F. Quncke, Ber. 21, 1454 (1888).
4. C. Graebe and N. Brions, Lieb. Ann. 327, 77 (1903).

* Institute of Chemical Reagents.

SYNTHESIS OF VINYL MONOMERS

IX. ANHYDRIDES OF METHACRYLIC ACID

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Mixed anhydrides can be obtained by reaction of the acid chloride of the acid with the anhydrous salt of another acid [1-4]; by the action of a mixture of the acid chloride and the anhydride of another acid on a salt of the acid [2]; by acylation of the acid by the acid chloride of another acid in the presence of a tertiary amine [3, 5, 6], or in its absence [7]; by acylation of the acid by the anhydride of another acid [8, 9].

Our objective was to obtain certain mixed anhydrides of methacrylic acid of interest in polymer synthesis. An attempt to obtain acetic methacrylic anhydride by reaction of sodium acetate with methacrylic chloride was unsuccessful, since at the reaction temperature (boiling in benzene) the mixed anhydride formed was completely resolved into its constituent acids. Because of this, the method of synthesis chosen was the acylation of methacrylic acid in ether by acetyl chloride in the presence of pyridine.

After suitable treatment, the remaining undistilled anhydride had a freezing point of about − 34° C. On distillation it passed over in the range 35-64° (3 mm), but, since the distillate obtained did not freeze even at −80°, it may be assumed that complete resolution of the anhydride took place during distillation. Purer acetic-methacrylic anhydride with freezing point − 28° was obtained by recrystallization from alcohol at −70° to −80°, this being accompanied, however, by poor recovery of the substance.

We repeated the synthesis of formic-acrylic and methacrylic anhydrides described by Barnes [11] (boiling sodium formate and methacrylic chloride in ether). However, no anhydride was observed in the reaction mixture after 5 or 20 hours' boiling. During attempts to obtain this anhydride from methacrylic chloride and formic acid in ether in the presence of pyridine, carbon monoxide was evolved, even with intense cooling, and methacrylic acid was found in the ethereal solution (in small quantities only). We obtained a mixed formic-methacrylic anhydride by reaction of methacrylic anhydride with anhydrous formic acid, using the method proposed for preparation of formic-acetic anhydride [9]. It distilled at 26° (1 mm) and had a freezing point of about − 50°. This anhydride, like acetic formic anhydride, on heating or on being reacted with pyridine, sodium acetate, sodium formate, etc., decomposed with formation of carbon monoxide and methacrylic acid. The properties of formic-methacrylic anhydride described indicate that this compound was not obtained by Barnes, and that the substance with b. p. 68-70° (12 mm), and m. p. 8°, accepted by him as this anhydride, was evidently impure methacrylic acid (b. p. 72.7° at 20 mm [12], m. p. 16°).

We obtained methacrylic anhydride for use in formic-methacrylic anhydride synthesis by reacting methacrylic acid with methacrylic chloride in the presence of pyridine, a yield of 75-80% being obtained. This method is different from that described in [13].

EXPERIMENTAL

Methacrylic anhydride. 90 g (1.04 moles) of methacrylic acid in 250 ml of absolute ether was placed in a flask, 0.1 g of cuprous chloride added, followed by 95 g (1.2 moles)of pyridine. 104.5 g (1 mole) of

methacrylic chloride was slowly added to the mixture with stirring and cooling to 0-5°, stirring being then continued at room temperature for 1 hour. The precipitated pyridine hydrochloride was filtered off; the ethereal solution was washed twice with dilute (1 : 4) hydrochloric acid cooled to 0°, twice with a cooled sodium bicarbonate solution, and then dried over calcium chloride. The ether was evaporated off, and the residue distilled. Yield was 110-120 g (72-78%).

B. p. 63-65° (2 mm), f. p. about − 20°; $n^{20}D$ 1.4530.

Acetic-methacrylic anhydride. 40 g (0.47 mole) of methacrylic acid, 40 g (0.51 mole) of acetyl chloride, and 45 g (0.57 mole) of pyridine in 150 ml of absolute ether, were used in the reaction. The reaction was carried out as described in the preceding experiment. Yield, 45 g (75%).

F. p. about − 34°; $n^{20}D$ 1.4230, d^{20}_4 1.0401.

15 g of crude acetic-methacrylic anhydride at room temperature was rapidly mixed with twice its volume of absolute alcohol, and the solution cooled to − 80°. The precipitated crystals were filtered off using a funnel cooled with a mixture of dry ice and acetone. After removal of the mother liquor, cooling of the funnel was discontinued, and the melted acetic-methacrylic anhydride run into a separate container. The remaining alcohol was removed under vacuum. Yield, 7.5 g.

F. p. − 28°, $n^{20}D$ 1.4253, d^{20}_4 1.0421, MR_D 31.43. $C_6H_8O_3F$. Calculated 31.06.

Found %: C 56.15, 55.82; H 6.62, 6.74. $C_6H_8O_3$. Calculated %: C 56.25; H 6.35.

Properties

A colorless, mobile, lachrymatory liquid with a strong odor. Miscible with alcohol and ether; soluble in petroleum ether, but separating out as an oil on cooling. Its freezing point was depressed on standing, even at room temperature, the refractive index also changing.

Formic-methacrylic anhydride. 69 g (0.45 mole) of methacrylic anhydride and 25 g (0.55 mole) of anhydrous formic acid were heated at 35-40° for 10-15 hours in the presence of a small quantity of inhibitor (hydroquinone). During the course of the reaction, carbon monoxide evolution was observed, occurring as a result of partial decomposition of the formic-methacrylic anhydride being formed. The refractive index of the mixture was lowered on reacting further, completion of the reaction being indicated by cessation of this lowering. Methacrylic acid formed as a decomposition product and, with the excess formic acid, were both removed by freezing to − 30°, the mother liquor then being distilled from a flask fitted with a fractionating column. The fraction passing over at 26-27° (1 mm) was collected. Yield, 25 g (49%).

F. p. about − 50°, $n^{20}D$ 1.4262, d^{20}_4 1.0941, MR_D 26.71. $C_5H_6O_3F$. Calculated 26.49.

Found %: C 52.61, 51.79; H 5.74, 5.67. $C_5H_6O_3$. Calculated %: C 52.63; H 5.30.

Properties

A colorless, mobile liquid with a pungent odor. When gently heated or when acted upon by reagents of an alkaline character, it decomposed with formation of carbon monoxide and methacrylic acid.

SUMMARY

The synthesis and properties of formic-methacrylic, acetic-methacrylic, and methacrylic anhydrides are described.

LITERATURE CITED

1. Gerhardt, Lieb. Ann. 82, 132 (1852); 83, 112 (1852).
2. A. Baroni, G. Marrano, and Modigliani, Gazz. 63, 23 (1933).
3. C. R. Noller and R. Adams, J. Am. Chem. Soc. 46, 1889 (1924).
4. A. W. Ralston and R. A. Reck, J. Org. Chem. 11, 624 (1946).

5. J. R. Vaughan, Jr. and R. L. Osato, J. Am. Chem. Soc. 74, 676 (1952); D. S. Tarbell and J. A. Price, J. Org. Chem. 22, 245 (1957); T. Wieland and D. Stimmung, Lieb. Ann. 579, 97 (1953).
6. A. Eingorn and R. Seuffert, Ber. 43, 2993 (1910).
7. F. Henle, Lieb. Ann. 348, 19 (1906).
8. K. Freudenberg and W. Jacob, Ber. 80, 325 (1947).
9. German Patent 113,165 (1899); Zbl. (1899), II, 181.
10. C. D. Hurd and M. E. Dull, J. Am. Chem. Soc. 54, 3427 (1932); R. Dunbar and F. Garven, Proc. N. Dakota Acad. Sci. 3, 24 (1949); Chem. Abs. 44, 5313 (1950); U. S. Patent 2,476,859 (1949); Chem. Abs. 43, 8398 (1949).
11. U. S. Patent 2,259,512 (1942); Chem. Abs. 36, 497 (1942); British Patent 569,433 (1945); Chem. Abs. 41, 5339 (1947).
12. D. R. Stell, Vapor Pressure Tables for Individual Substances [in Russian] (Moscow, 1949).
13. A. A. Berlin and T. A. Makarova, Zhur. Obshch. Khim. 21, 1271 (1951);* I. A. Arbuzova, S. A. Plotkina, and V. N. Efimova, Zhur. Obshch. Khim. 26, 1124 (1956);* British Patent 538,310 (1941); Chem. Abs. 36, 1613 (1942); U. S. Patent 2,143,924; Chem. Abs. 33, 2913 (1939).

* Original Russian pagination. See C. B. translation.

MECHANISM OF THE REACTION BETWEEN NITRILES, CARBOXYLIC ACIDS AND HYDROGEN CHLORIDE AT LOW TEMPERATURE

E. N. Zil'berman

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Recently it was shown that the chlorides of imonium chlorides, obtained from nitriles and hydrogen chloride, are extremely reactive compounds. They readily react with water in the cold to form imonium hydrin chlorides (amide hydrochlorides) [1], and with primary alcohols to form the hydrochlorides of imino esters [2].

Colson [3, 4] described the preparation of some amide hydrohalides and acid halides from equimolar amounts of acid and nitrile in the presence of hydrogen halide at 0°, in accordance with Eq. (1).

$$RCN + R'COOH + 2HCl \longrightarrow RCONH_2 \cdot HCl + R'COCl \qquad (1)$$

Colson assumed that the acid reacts first with the hydrogen chloride to form acyl chloride and water, and then the water adds to the nitrile.

To obtain the anhydrides of chloroacetic acids it has been proposed [5] to react hydrocyanic acid with chloro-substituted acetic acids in an organic solvent in the presence of a hydrogen halide.

$$HCN + 2R'COOH \xrightarrow{HCl} HCONH_2 + (R'CO)_2O \qquad (2)$$

Imino chloride H(Cl)C=NH and secondary amide HCONHCOR' are assumed to be the intermediate products in this reaction.

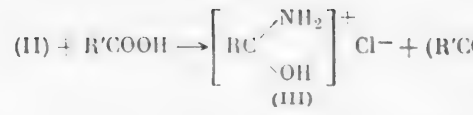
In this paper, we investigated the reaction of the chlorides of imonium chlorides with carboxylic acids in an organic solvent. We postulated that in the investigated reaction between nitriles, carboxylic acids and hydrogen chloride the initially formed chlorides of imonium chlorides (I), as the result of subsequent bimolecular replacement, migrate to relatively unstable isoimide salts (II). Since the latter should possess a substantial acylating capacity, they react with carboxylic acids to form imonium hydrin chlorides (III) and acid anhydrides. The acid chlorides can be obtained by secondary reaction between the acid anhydrides and hydrogen chloride [4], and possibly also by the acylation of hydrogen chloride with the isoimide.

$$RCN + 2HCl \rightleftarrows \underset{(I)}{\left[RC(=NH_2)Cl\right]^+ Cl^-} \qquad (3)$$

$$(I) + R'COOH \rightleftarrows \left[RC(=NH_2)OCOR'\right]^+ Cl^- + HCl \qquad (4)$$

$$\downarrow (II)$$

$$RCN + R'COOH + HCl$$



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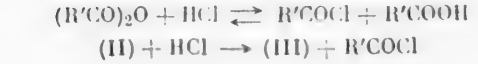
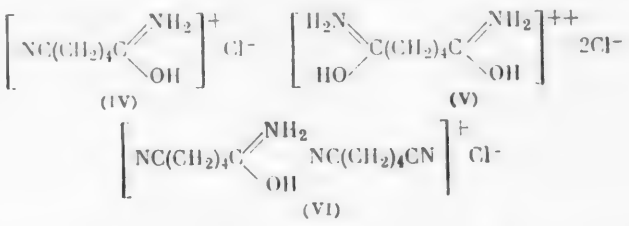


(7)

To verify the mechanism proposed for the initial stage of the reaction (3, 4) we investigated the reaction of acetic acid with adiponitrile in the presence of hydrogen chloride. Adiponitrile proved to be highly satisfactory for this purpose, since together with imonium hydrin chlorides (IV) and (V) it also gives [1] molecular compound (VI), which makes it possible to show the presence of free nitrile in the reaction mixture.



The reaction was run in both polar and nonpolar organic solvents. As can be seen from the data in the table, the amount of precipitate increases with increase in the amount of excess hydrogen chloride, accompanied by an increase in the amount of (V) contained in it, which indicates the equilibrium character of Reaction (3). It should be mentioned that even with a large excess of HCl it proves impossible to attain a yield of the amide that is close to the theoretical, although there is a nearly quantitative conversion of the reagents, even in the absence of excess hydrogen chloride, when these same chlorides of imonium chlorides (I) are reacted with water or with primary alcohols. This is best explained by the fact that isoimide hydrochloride (II), in contrast to the corresponding products obtained when reaction is with water or with alcohols, does not deposit in the precipitate and consequently is not removed from the reaction zone, but instead partially decomposes into nitrile and acid (4). In addition, as is known [6], acetic acid is capable of accepting protons. Consequently, it must be assumed that it reacts with (I) not only according to Reaction (4), but also that it cleaves a proton from (I), simultaneously shifting the equilibrium of Reaction (3) to the left.

If this assumption is correct, then the character of the reaction of acetic acid with the chloride of the imonium chloride (I) should be the same as when reaction is with water [1], which in large excess promotes the dissociation of (I), while in small amounts it reacts with (I) with the formation of the imonium hydrin chloride. Experiments 4 and 6-8 (see table) revealed that increasing the amount of acetic acid relative to the adiponitrile initially accelerates reaction. With further increase in the amount of excess acetic acid the reaction slows down, while the relative amount of molecular compound (VI) in the reaction products increases.

To prove that secondary amides are not formed under our experimental conditions, but that the acylating agent is isoamide (II), we studied the reaction of acetonitrile with butyric acid, and of butyronitrile with acetic acid, in the presence of hydrogen chloride. If the secondary amide, $CH_3CONHCOCH_2CH_2CH_3$, was to be found present in the reaction mixtures, then as the result of acylation [7] both the chloride of the imonium hydrin of acetic acid (VII) and the chloride of the imonium hydrin of butyric acid (VIII) would be obtained in both cases. Actually, the precipitate from the experiment with acetonitrile contained only (VII), while the precipitate from the experiment with butyronitrile contained only the previously unknown (VIII). In addition, quite recently, it was shown [8] that N-substituted isoimides are capable of acylating carboxylic acids, and that N-substituted secondary amides are much weaker acylating agents than the corresponding isoimides. Consequently, contrary to [5], secondary amides are not intermediate products in the examined reaction. It is possible to obtain secondary amides from nitriles and acids only under much more drastic conditions.

In investigating the liquid products it was found that these same carboxylic acids are converted not only to acid chlorides, as was indicated earlier [3, 4], but also to the acid anhydrides [5].

Utilization of the discovered rules regarding the favorable influence exerted by a stoichiometric excess of hydrogen chloride and the existence of an optimum ratio between nitriles and carboxylic acids when they are reacted in the cold makes it possible in a number of cases to obtain the imonium hydrin chlorides (III) in high yields. Thus, if a 65% yield of (VII) is obtained from equimolar amounts of acetonitrile and acetic acid, then under identical conditions and with the same excess of HCl, but using a 1 : 2 molar ratio of acetonitrile to acetic acid, the yield of (VII) was 87%.

Effect of Ratio of Components on the Formation of Amides in the Reaction of Adiponitrile With Acetic Acid

Expt. No.	Starting components (in moles)		Weight of precipitate (in g)	Amount in precipitate (in wt. %)			Yield of amides (in %)	Isolated in hydrolysis of the precipitate (in g)		
	Hydrogen chloride	Acetic acid		Chlorine	Nitrile nitrogen	Amide nitrogen		δ-Cyanovaleramide	Adipamide	Adiponitrile
1	0.2	0.2	1.15	13.0	15.2	4.9	2	0.5	—	0.3
2	0.25	0.2	2.8	17.9	12.2	7.0	7			
3	0.5	0.2	11.1	20.1	9.4	7.8	30	5.5	1.0	1.6
4	0.75	0.2	15.0	23.6	7.2	9.2	49			
5	1.0	0.2	16.3	24.9	6.6	9.4	55	3.2	5.9	1.8
6	0.75	0.13	8.0	22.5	8.0	8.4	24			
7	0.75	0.35	14.6	24.0	6.3	9.4	49			
8	0.75	0.5	8.4	19.8	10.1	7.9	24			

Remarks. Temperature − 5 to 0°, time 13-16 days, 0.1 mole of adiponitrile, 60 ml of ether.

In conclusion the author wishes to thank M. M. Bershtein for his assistance in making the study.

EXPERIMENTAL

All of the reagents and solvents used in the work were dried until all moisture was absent. The acetonitrile, butyronitrile and butyric acid had respectively, b. p. 81.5, 117, and 162°, and $n^{20}D$ 1.3992, 1.3833, and 1.3442. The constants of adiponitrile were given earlier [9]. The solid reaction products were analyzed in the same manner as described in a previous paper [1].

Reaction of adiponitrile with acetic acid. With stirring and cooling to 0°, 120 g (3.3 moles) of dry HCl was passed into a mixture of 43.2 g (0.4 mole) of adiponitrile and 250 ml of dioxane. The next day, 48 g (0.8 mole) of glacial acetic acid was added to the mixture and the whole allowed to stand at − 5 to 0°. After 14 days the precipitate (60.1 g) was filtered, proving to be a mixture of chlorides (IV-VI), and analyzing 24.7% chlorine, 6.4% nitrile nitrogen, and 9.6% amide nitrogen. The precipitate was washed well with benzene. We isolated 8 g of adiponitrile from the wash liquor. The residue was placed in 200 ml of water and neutralized with 10% caustic solution. The obtained adipamide (m. p. 224°) was filtered, and the mother liquor was evaporated to dryness. Extraction of this residue with boiling ethyl acetate gave 13.4 g (27.6%) of δ-cyanovaleramide (m. p. 64°). The portion insoluble in ethyl acetate was a mixture of NaCl and adipamide. The total yield of adipamide was 20.1 g (35%). The obtained amides were identical with the earlier described compounds [1].

Fractional distillation of the dioxane filtrate through a column gave 7.8 g of acetyl chloride with b. p. 45-55°, which was reacted with aniline to give acetanilide with m. p. 114°; the mixed melting point with an authentic specimen was not depressed. The next fraction (55-101°) weighed 49 g and contained 12.2% of acetyl chloride, isolated as acetanilide. The total yield of acetyl chloride was 22% based on the starting acetic acid, i.e., 0.43 equiv. of acid chloride was isolated per equivalent of amide formed. Treatment of the residue in the distillation flask with aniline led to the isolation of acetanilide (m. p. 114°), which testifies to the presence

of acetic anhydride in the reaction products. In the experiments with acetic acid we obtained precipitates during the distillation, which subsequently disappeared, in which connection the reaction mixture turned either brown or black. All of this indicates that the composition of the product being distilled changed during distillation, as a result of which the acetic anhydride was not isolated quantitatively.

Reaction of acetonitrile with butyric acid. With stirring and cooling to 0°, 90 g of HCl was passed in 3 hours into a solution of 16.4 g (0.4 mole) of acetonitrile and 70.4 g (0.8 mole) of butyric acid in 100 ml of benzene, and then the whole was allowed to stand in the cold. After 13 days the precipitate was filtered and washed with ether to give 34.5 g (90%) of the chloride of the imonium hydrin of acetic acid (VII), m. p. 140-142° (decomp.), which on hydrolysis gave acetamide.

Found %: Cl 37.0; N 14.7. C_2H_6ONCl. Calculated %: Cl 37.1; N 14.7.

The mother liquor was fractionally distilled. After removal of the HCl at atmospheric pressure, the 1st fraction was collected with b. p. up to 90°. This fraction weighed 84.4 g and after hydrolysis was found to contain 7% chlorine by silver nitrate titration. Five grams of this fraction was treated in the cold with 3 g of aniline. The benzene was distilled off and the residue was washed with water to give 1.65 g of butyranilide, m. p. 92° (from water). The mixed melting point with authentic butyranilide was not depressed. Consequently, the 1st fraction contained 21.5% of butyryl chloride. The next, intermediate fraction (8 g) was distilled at 100 mm, gradually raising the temperature to 75°. Using aniline it was found that this fraction contains 24% of butyryl chloride. From the difference between the total acidity and the acidity due to the acid chloride, we determined that this fraction contains 26.5% of butyric acid. The last fraction (39.4 g) was distilled at a pressure of 35 mm and a final vapor temperature of 107°. This fraction was devoid of chlorine. The reaction of 2 g of this fraction with aniline gave 1.4 g of butyranilide, which corresponds to a 62% content of butyric anhydride in this fraction. The residue proved to be unreacted butyric acid. As a result, the yield of distilled butyryl chloride and butyric anhydride was, respectively, 24 and 39%, based on starting butyric acid.

Reaction of butyronitrile with acetic acid. In a similar manner, from 6.9 g (0.1 mole) of butyronitrile, 12 g (0.2 mole) of acetic acid and 29 g (0.8 mole) of HCl in 40 ml of benzene, after allowing to stand for 14 days, we obtained 4 g of the chloride of the imonium hydrin of butyric acid (VIII) as long needles with m. p. 83-84° (from a mixture of acetic acid and ether). Allowing the filtrate to stand for another 12 days at the same temperature gave an additional 1.7 g of (VIII). Total yield 46%.

Found %: Cl 28.4; N 11.3. $C_4H_{10}ONCl$. Calculated %: Cl 28.6; N 11.4.

A solution of 1.3 g of the obtained crystals in 3 ml of water was neutralized with sodium carbonate. The solution was evaporated and extraction of the residue with acetonitrile led to the isolation of butyramide, m. p. 113°; literature data [10]: m. p. 115-116°.

Reaction of acetonitrile with acetic acid. From a mixture of 8.2 g (0.2 mole) of acetonitrile, 12 g (0.2 mole) of acetic acid and 58 g (1.6 moles) of hydrogen chloride in 80 ml of toluene, after allowing to stand for 18 days, we obtained 12.4 g (65%) of the chloride of the imonium hydrin of acetic acid (VII), m. p. 140-142° (decomp.). Distillation of the filtrate gave 4.6 g (29%) of acetyl chloride (based on the starting acetic acid).

In a parallel experiment, but using 24 g of acetic acid (instead of 12 g), we obtained 16.6 g (87%) of (VII).

SUMMARY

A study was made of the effect of the ratios of the reactants on the reaction of nitriles, carboxylic acids and hydrogen chloride at 0° in organic solvents. Based on the obtained results, a mechanism was proposed for this reaction, according to which the initially formed chloride of the imonium chloride is converted to the isoimide by reaction with the carboxylic acid. The isoimide then acylates a second molecule of the carboxylic acid with the formation of the chloride of the imonium hydrin (amide hydrochloride) and the acid anhydride.

LITERATURE CITED

1. E. N. Zil'berman and A. E. Kulikova, Zhur. Obshch. Khim. 29, 1694 (1959).*

* Original Russian pagination. See C. B. translation.

2. E. N. Zil'berman and A. E. Kulikova, Zhur. Obshch. Khim. 29, 3039 (1959).*
3. A. Colson, Compt. rend. 121, 1155 (1895).
4. A. Colson, Ann. chim. et Phys. [7] 12, 231 (1897).
5. U. S. Patent 2,390,106 (1945); Chem. Abs. 40, 1868 (1946).
6. L. F. Audrieth and J. Kleinberg, Nonaqueous Solvents [Russian translation] (IL, 1955), p. 173.
7. T. Wieland and H. Mohr, Ann. 599, 222 (1956).
8. C. L. Stevens and M. E. Munk, J. Am. Chem. Soc. 80, 4065 (1958).
9. A. E. Kulikova, E. N. Zil'berman, Ts. N. Roginskaya, and M. M. Smirnova, Zhur. Priklad. Khim. 32, 227 (1959).*
10. Dictionary of Organic Compounds [Russian translation] Vol. 1, p. 373.

* Original Russian pagination. See C. B. translation.

PREPARATION OF SOME N-OXIDES OF ARYLALKYL AMINES

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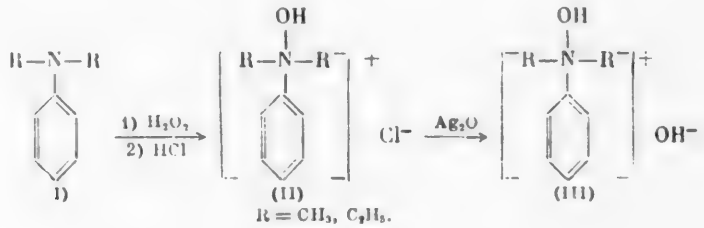
Data exist that cancer cells are more sensitive to oxidizing agents than are normal cells [1]. In connection with this it seemed of interest to synthesize the N-oxides of some tertiary amines, in order to investigate their antitumor activity.

A method for obtaining the N-oxides of arylalkyl amines was worked out by Bamberger [2]. By oxidizing dimethylaniline with 3% hydrogen peroxide the author obtained dimethylaniline N-oxide as the picrate in nearly quantitative yield; however, isolation of the oxide hydrochloride and of the N-oxide itself from the picrate is described without any indication of the yield. Later V. N. Belov and K. K. Savich [3] reported that they were unable to isolate the pure dimethylaniline N-oxide when operating as described by Bamberger. The corresponding N-oxides are formed in poor yield (isolated as the picrates) when diethylaniline, dimethyl-o-toluidine, dimethyl-p-toluidine, etc., are oxidized for a long time (250-300 hours).

When dimethylaniline (I, R = CH_3) was oxidized by the Bamberger method with 3% hydrogen peroxide we obtained a 61% yield of dimethylaniline N-oxide hydrochloride (II, R = CH_3); however, we were unable to isolate the hydrochloride of diethylaniline N-oxide in this manner.



R = CH_3, C_2H_5.

On the assumption that the unsatisfactory results obtained in the oxidation of the above amines are due to the low solubility of the amines in water, we examined the oxidation of the amines with hydrogen peroxide in a mixture of water and dioxane and found that the reaction goes much more smoothly if this solvent mixture is taken in a 1:1 ratio.

Using this technique, we obtained the pure hydrochloride of diethylaniline N-oxide (II, R = C_2H_5) in good yield from diethylaniline (I, R = C_2H_5). Treatment of the hydrochloride with moist silver oxide gave diethylaniline N-oxide monohydrate (III, R = C_2H_5).

The oxidation of dimethyl-o-toluidine gave dimethyl-o-toluidine N-oxide hydrochloride in good yield. We were unable to convert 5-dimethylamino-4-methyluracil [5], obtained by reacting 5-bromo-4-methyluracil [4] with dimethylamine, to the N-oxide, either by treatment with 3% hydrogen peroxide in a mixture of dioxane and water or by reaction with a 45% solution of hydrogen peroxide in acetic anhydride.

Testing of the N-oxides for their antitumor activity (done by E. M. Shamaeva and A. E. Markitantova) revealed that the hydrochloride of dimethyl-o-toluidine N-oxide suppresses the growth of rat sarcoma 45 very slightly and inhibits the growth of Ehrlich tumors to the extent of 36%. The hydrochloride of diethylaniline N-oxide exerts a somewhat stimulating effect on the growth of both rat sarcoma 45 and Ehrlich tumors.

5-Dimethylamino-4-methyluracil fails to show any antitumor activity against rat sarcoma 45 (testing done by E. I. Khomchenovskii).

EXPERIMENTAL*

Dimethylaniline N-oxide hydrochloride (II, R = CH_3). A mixture of 10 g of dimethylaniline (0.082 mole) and 280 ml of 3.2% hydrogen peroxide (0.27 mole) was placed in a three-necked flask, fitted with a reflux condenser, thermometer, and Hershberg stirrer. The mixture was heated on the water bath at 70-80° for 8 hours with vigorous stirring. The obtained yellow solution was extracted with ether, acidified with HCl until acid to Congo, and then evaporated at 10-15 mm.

Recrystallization of the residue from acetone gave 8.5 g (61.4%) of the N-oxide salt as colorless needles, melting at 122-124° (with decomp.). From the literature [2]: m. p. 124-125°.

Diethylaniline N-oxide hydrochloride (II, R = C_2H_5). A mixture of 15 g (0.1 mole) of diethylaniline and 300 ml of 3.2% hydrogen peroxide (0.3 mole) in a mixture of dioxane and water (1:1) was heated with stirring for 48 hours on the water bath at 70-80°. The red-orange solution was diluted with 450 ml of water and extracted with ether. The aqueous dioxane solution was acidified with HCl until acid to Congo and then it was evaporated in vacuo. The residue was a viscous yellowish oil that crystallized when rubbed. Recrystallization from dioxane gave 11.8 g (57.9%) of the N-oxide hydrochloride as colorless prisms with m. p. 130-131°.

Found %: C 59.80; H 8.33; N 6.69. $C_{10}H_{16}ONCl$. Calculated %: C 59.54; H 8.00; N 6.95.

Diethylaniline N-oxide monohydrate (III, R = C_2H_5). Two grams (0.01 mole) of (II, R = C_2H_5) was triturated with 2 g (0.009 mole) of silver oxide in 4 ml of water, after which the silver chloride was filtered and the filtrate was evaporated to dryness at room temperature in a vacuum-desiccator (over P_2O_5). The residue, a nearly colorless sirup, crystallized when triturated with 2-3 ml of absolute ether. Weight 1.38 g (76%). Recrystallization from a mixture of anhydrous alcohol and ether gave colorless plates with m. p. 92-92.5°.

Found %: C 65.73; H 9.35; N 7.42. $C_{10}H_{17}O_2N$. Calculated %: C 65.54; H 9.35; N 7.67.

Dimethyl-o-toluidine N-oxide hydrochloride. A mixture of 12 g (0.088 mole) of dimethyl-o-toluidine [6] and 300 ml of 3.2% hydrogen peroxide (0.3 mole) in a mixture of dioxane and water was heated with stirring for 60 hours at 70-80°. Then the solution was worked up in the same manner as described for the hydrochloride of diethylaniline N-oxide. Recrystallization from a mixture of alcohol and ether gave 9.7 g (58.2%) of colorless needles with m. p. 138-139°.

Found %: C 57.43; H 7.72; N 7.65; Cl 19.01. $C_{10}H_{14}ONCl$. Calculated %: C 57.60; H 7.52; N 7.47; Cl 18.89.

5-Dimethylamino-4-methyluracil. To an efficiently stirred suspension of 40 g (0.31 mole) of 4-methyluracil in 130 ml of CCl_4 was slowly added 125.6 g (0.78 mole) of bromine. The obtained red precipitate was filtered and then debrominated by heating in a porcelain dish on the water bath until it changed to a pale yellow powder. Recrystallization from water gave 56.3 g of 5-bromo-4-methyluracil (86.8% yield) as colorless needles with m. p. 238-240°.

Found %: C 29.34; H 2.39; N 13.59. $C_5H_5O_2N_2Br$. Calculated %: C 29.29; H 2.46; N 13.67.

A solution of 280 g (1.36 mole) of 5-bromo-4-methyluracil in 1200 ml of 33% aqueous dimethylamine (7.28 mole) was loaded in equal portions into 14 acid-resistant stainless steel tubes and then heated in an oil bath for 3.5 hours at 150°, and for 2.5 hours at 175°. The obtained colorless, lustrous, scaly crystals were filtered

* The microanalyses were run under the supervision of A. D. Chinaeva.

and washed with water, and then with ethanol. We obtained 131.5 g of substance with m. p. 285-295° (decomp.). An additional 28.8 g of substance with m. p. 294-298° was isolated from the mother liquor. Yield 70%. Recrystallization from 80% aqueous alcohol gave the 5-dimethylamino-4-methyluracil as scintillating, colorless needles with m. p. 295-298°.

Found %: C 49.86; H 6.64; N 24.61. $C_7H_{11}O_2N_3$. Calculated %: C 49.69; H 6.56; N 24.84.

5-Dimethylamino-4-methyluracil hydrochloride monohydrate. A strong heating up of the reaction mixture was observed when 1 g (0.0048 mole) of 5-dimethylamino-4-methyluracil was mixed with 1.5 ml (0.014 mole) of concentrated HCl, and a finely crystalline precipitate was obtained. We obtained 0.69 g of the salt with m. p. 253-255°.

Found %: C 38.11; H 6.47; N 19.26; Cl 15.87. $C_7H_{14}O_3N_3Cl$. Calculated %: C 37.58; H 6.31; N 18.79; Cl 15.85.

SUMMARY

1. In developing the Bamberger method for the oxidation of tertiary amines we worked out a convenient technique for obtaining the N-oxides of tertiary arylalkyl amines, consisting in the oxidation of the amines with 3% hydrogen peroxide in a mixture of dioxane and water. With this technique we obtained diethylaniline N-oxide monohydrate and dimethyl-o-toluidine N-oxide hydrochloride in good yield.

2. The reaction of 5-bromo-4-methyluracil with dimethylamine gave 5-dimethylamino-4-methyluracil.

LITERATURE CITED

1. J. Sclomides and E. Ronsin, Parfumerie mod. 45, 82 (1953).
2. E. Bamberger and F. Tschirner, Ber. 32, 342, 1882 (1899); E. Bamberger and P. Leyden, Ber. 34, 12 (1901).
3. V. N. Belov and K. K. Savich, Zhur. Obshch. Khim. 17, 257 (1947).
4. R. Behrend, Ann. 229, 1 (1885); 231, 249 (1885); Org. Syntheses [Russian translation] Collection (1949), Vol. 2, p. 335.
5. H. L. Wheeler and G. S. Jamieson, Am. Chem. J. 32, 355 (1904); T. B. Johnson and I. Matsuo, J. Am. Chem. Soc. 16, 782 (1919).
6. H. Reinhardt and W. Staedel, Ber. 16, 29 (1883).

ESTERS OF ARYLFLUORO- AND ARYLFLUOROTHIOPHOSPHINIC ACIDS

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The use of alkylfluorophosphinic acid derivatives as insecticides is prevented by their high toxicity to warm blooded animals. Replacing the alkyl by aryl usually reduces the toxicity of the compounds. In this paper we synthesized some esters of arylfluoro- and arylfluorothiophosphinic acids for the purpose of studying their insecticidal properties. The arylphosphinic difluorides needed for the syntheses were described by us earlier [1]. The arylthiophosphinic difluorides were obtained in good yields from the corresponding dichlorides by reaction with zinc fluoride: the reaction began after gentle warming and went briskly with much evolution of heat. Phenylthiophosphinic difluoride was obtained in much smaller yield by replacing the oxygen in phenylphosphinic difluoride by sulfur using phosphorus pentasulfide [2].

$$\underset{(I)}{C_6H_5POF_2} \xrightarrow{P_2S_5} \underset{(II)}{C_6H_5PSF_2}$$

The low yield of (II) (25%) is apparently due to a partial decomposition of the easily hydrolyzed (I) when heated for a long time in glass apparatus at 160°. The fluorination of the arylthiophosphinic dichlorides with antimony trifluoride gave the arylthiophosphinic difluorides in low yields, since a large amount of sulfur-containing antimony compounds was formed as the result of side reactions.

TABLE 1

Arylthiophosphinic Difluorides $RC_6H_4P(S)F_2$

R	Boiling point	Yield (in %)	d_4^{20}	n_D^{20}	Empirical formula	MR_D Found	MR_D Calc.	%P Found	%P Calc.
H	187—188°	89.6	1.3015	1.5260*	$C_6H_5PSF_2$	41.97	42.01	17.73, 17.51	17.42
CH_3	208—209	73.6	1.2543	1.5180	$C_7H_7PSF_2$	46.39	46.54	16.05, 16.24	16.14
Cl	103—105(20)	68.6	1.4324	1.5470	$C_6H_4PSF_2Cl$	47.07	46.87	14.35, 14.25	14.59

* Freshly distilled phenylphosphinic difluoride has $n^{18}D$ 1.4650, but this changes rapidly as the result of hydrolysis of the compound by atmospheric moisture.

The arylthiophosphinic difluorides are colorless, heavy oils with a characteristic odor, and soluble in most organic solvents. In contrast to the arylphosphinic difluorides, which are hydrolyzed by water with the evolution of heat, the arylthiophosphinic difluorides are not decomposed by water even when heated. In their boiling points they do not differ from the corresponding oxygen analogs, while the densities and refractive indices are somewhat higher for the corresponding thio derivatives. The synthesized compounds, their constants, and the analysis data are all given in Table 1.

The atomic refraction data for the alkylphosphinic acids [3] was used in calculating the molecular refractions.

The fluorine atoms in the aryl- and arylthiophosphinic difluorides do not have the same chemical activity. This made it possible for us to obtain a series of esters of the arylfluoro- and arylfluorothiophosphinic acids. The obtained esters, their constants, and the analysis data are summarized in Table 2.

TABLE 2

Esters of Phenylfluorophosphinic Acid $C_6H_5P(O)F(OR)$

R	Boiling point (pressure in mm)	Yield (in %)	d_{20}^{18}	n_D^{18}	Empirical formula	MR_D		%P		%F	
						Found	Calc.	Found	Calc.	Found	Calc.
CH_3	85—86° (4)	56.6	1.2469	1.4896	$C_7H_8O_2PF$	40.22	40.13	18.00, 17.95	17.82	10.78, 11.04	10.92
C_2H_5	95 (2)	64.7	1.1911	1.4835	$C_8H_{10}O_2PF$	45.12	44.75	16.25, 16.12	16.45	10.18, 9.95	10.10
iso-C_3H_7	133—134 (18)	84.7	1.1480	1.4770	$C_9H_{12}O_2PF$	49.73	49.37	15.21, 15.51	15.35	9.42, 9.69	9.41

The esters of the arylfluorothiophosphinic acids were obtained by reacting the appropriate difluorides with alcohols in the presence of triethylamine, and also by reacting the difluorides with alcohol solutions of the alcoholates or with the dry phenolates. The esters are colorless liquids, are soluble in most organic solvents, and have boiling points that are quite close to those of the oxygen analogs. They are insoluble in water, and do not hydrolyze even when heated.

The formation of a mercaptan, the amount of which increased if the reaction was run at 50°, was observed in the preparation of the methyl esters of phenyl- and p-tolylfluorothiophosphinic acids.

The obtained esters, their constants, and the analysis data are summarized in Table 3.

All of the compounds synthesized by us proved to be good insecticides. The toxicity of some of the arylfluorothiophosphinic esters to warm blooded animals does not exceed the toxicity of currently used organophosphorus insecticides.

EXPERIMENTAL

The thiophosphinic dichlorides were obtained from the corresponding dichlorophosphines by the addition of sulfur in the presence of aluminum chloride [4].

p-Chlorophenylthiophosphinic dichloride. A mixture of 55.6 g of p-chlorophenyldichlorophosphine, 11.9 g of sulfur and 2.7 g of aluminum chloride in a Claisen flask, fitted with a column, was cautiously heated with a free flame for several minutes, and then the mixture was distilled. Yield 54.5 g (85.3%). B. p. 155° at 14 mm, $n^{18}D$ 1.6365, d^{18} 1.506.

Found %: P 14.35, 14.25. $C_6H_4PSCl_3$. Calculated %: P 14.59.

TABLE 3

Esters of Arylfluorothiophosphinic Acids $R'C_6H_4P(S)F(OR'')$

R′	R″	Boiling point (pressure in mm)	Yield (in %)	d	n_D	Empirical formula	MR_D		%P	
							Found	Calc.	Found	Calc.
H	CH_3	84—85°(4)	65.3	1.2415 (17.5°)	1.5421 (17.5°)	C_7H_8OPSF	48.12	48.45	16.23, 16.30	16.32
H	C_2H_5	100—101 (4)	54.7	1.1942 (18.5°)	1.5300 (18.5°)	$C_8H_{10}OPSF$	52.77	52.96	15.05, 15.55	15.20
H	iso-C_3H_7	104 (4)	82.5	1.1508 (20°)	1.5181 (20°)	$C_9H_{12}OPSF$	57.38	57.60	14.26, 14.01	14.21
H	C_6H_5	110—111 (0.25)*	75.7	1.2507 (18°)	1.5860 (18°)	$C_{12}H_{10}OPSF$	67.85	67.61	12.11, 12.23	12.30
H	SC_6H_4Cl-*n*	144—145 (0.2)**	62.5	—	—	$C_{12}H_9PS_2FCl$	—	—	10.00, 9.99	10.27
CH_3	CH_3	95 (2)	52.0	1.2096 (18°)	1.5372 (18°)	$C_8H_{10}OPSF$	52.70	53.09	14.72, 15.01	14.90
CH_3	C_2H_5	100 (2)	89.1	1.1686 (16°)	1.5282 (16°)	$C_9H_{12}OPSF$	57.46	57.70	14.00, 14.25	14.21
CH_3	iso-C_3H_7	106—108 (2)	89.4	1.1324 (17.5°)	1.5190 (17.5°)	$C_{10}H_{14}OPSF$	62.19	62.32	13.35, 13.56	13.36

* M. p. 25-26°. The MR_D was determined for the freshly distilled, not crystallized ester.
** M. p. 38-40°.

The dianilide was obtained as colorless needles. M. p. 158-159° (from aqueous alcohol).

Found %: P 8.77, 8.74. $C_{18}H_{16}N_2PSCl$. Calculated %: P 8.65.

Phenylthiophosphinic difluoride. Phenylthiophosphinic dichloride (27.4 g) was placed in a Wurtz flask and heated with a free flame nearly to the boil. Then 20 g of zinc fluoride was added in portions without admitting any air. At the end of reaction the product was vacuum-distilled using a water-jet pump and a strongly cooled receiver. Yield 21.1 g (89.6 %). B. p. 186-188°, or 82° at 20 mm.

The other arylthiophosphinic difluorides were obtained in a similar manner.

Methyl ester of phenylfluorophosphinic acid. To a solution of 7.2 g of phenylphosphinic difluoride in 20 ml of benzene was added in drops, with water cooling, a benzene solution of 1.8 ml of methyl alcohol and 6.2 ml of triethylamine at a temperature not exceeding 17°. The reaction mixture was allowed to stand overnight, after which the benzene solution was washed with water and dried. The benzene was distilled off, and the product was vacuum-distilled.

The same procedure was used to obtain the ethyl and isopropyl esters of phenylfluorophosphinic acid, the methyl and isopropyl esters of phenylfluorothiophosphinic acid, and also the esters of p-tolylfluorothiophosphinic acid.

Ethyl ester of phenylfluorothiophosphinic acid. A solution of 0.65 g of sodium in 14 ml of anhydrous alcohol was added in drops and with stirring to a solution of 5 g of phenylthiophosphinic difluoride in 20 ml of benzene in 5 minutes. Here the temperature rose to 40°. The reaction mixture was allowed to stand overnight, after which it was washed with water, dried, and vacuum-distilled.

Phenyl ester. A solution of 4.1 g of sodium phenolate in 60 ml of dry dioxane was added in drops, with stirring and ice water cooling, to a solution of 5.8 g of phenylthiophosphinic difluoride in 15 ml of dioxane. The reaction mixture was heated for 1 hour at 50°, after which it was diluted strongly with water, and the heavy oil layer of phenyl ester, collecting on the bottom of the separatory funnel, was washed several times with water, extracted with benzene, and the benzene solution was dried and then vacuum-distilled.

p-Chlorothiophenyl ester. A solution of 0.48 g of Na in 10 ml of anhydrous methanol was added to a solution of 3 g of p-chlorothiophenol in 20 ml of methanol. The alcohol was distilled on the water bath using the vacuum of a water-jet pump. The sodium thiophenolate was suspended in 100 ml of dioxane and added in portions to 3.7 g of phenylthiophosphinic difluoride. The mixture was allowed to stand overnight. Subsequent treatment was the same as already described for the preparation of the phenyl ester of phenylfluorothiophosphinic acid.

SUMMARY

The synthesis of the phenyl-, p-chlorophenyl- and p-tolylthiophosphinic difluorides was described. A number of esters of phenylfluorophosphinic acid and of phenyl- and p-tolylfluorothiophosphinic acids were prepared.

LITERATURE CITED

1. L. M. Yagupol'skii and Zh. M. Ivanova, Zhur. Obshch. Khim. 29, 3766 (1959).*
2. M. I. Kabachnik and N. N. Godovikov, Doklady Akad. Nauk SSSR 110, 217 (1956).*
3. M. I. Kabachnik, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk,(1948), p. 225.
4. British Patent 713,412 (1954); Chem. Zentr. (1955), p. 4212; Chem. Abs. 49, 2482i (1955).

* Original Russian pagination. See C. B. translation.

m- AND p-AMINOPHENYLETHYLENE GLYCOLS

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Recently the m- and p-nitrophenylchloromethylcarbinols became readily available compounds [1]. We decided to convert them to the m- and p-aminophenylethylene glycols, which could be useful in the synthesis of dyes and high-molecular compounds. The synthesis of the m- and p-nitrophenylethylene glycols was accomplished by heating the appropriate nitrophenylchloromethylcarbinols with aqueous potassium carbonate solution.

$$NO_2C_6H_4CHOHCH_2Cl \rightarrow \underset{(I)}{NO_2C_6H_4CHOHCH_2OH}$$

Both glycols are very soluble in water, for which reason after reaction they were extracted from the reaction mixture in an extractor using either ether or dichloroethane. m-Nitrophenylethylene glycol was also obtained by the hydrolysis of the diacetyl derivative (II) according to the scheme:

$$m\text{-}NO_2C_6H_4\underset{\underset{OCOCH_3}{|}}{CH}-CH_2Cl \xrightarrow{CH_3COOK} \underset{\underset{OCOCH_3}{|}}{m\text{-}NO_2C_6H_4CH}-CH_2OCOCH_3 \xrightarrow{H_2O}$$
$$\underset{(II)}{}$$
$$\rightarrow m\text{-}NO_2C_6H_4CHOHCH_2OH$$

p-Nitrophenylethylene glycol is obtained when p-nitrostyrene oxide is heated with 1% sulfuric acid. The hydration of m-nitrostyrene oxide is a much more complicated process. In this case, a large amount of by-products is formed, making isolation of the m-nitrophenylethylene glycol difficult.

The oxidation of p-nitrophenylethylene glycol with dilute nitric acid yields p-nitrobenzoylcarbinol (III) with m. p. 134-135°.

$$p\text{-}NO_2C_6H_4CHOHCH_2OH \rightarrow \underset{(III)}{p\text{-}NO_2C_6H_4COCH_2OH}$$

Engler and Zielke give a m. p. of 121° [2] for (III). The indicated authors obtained (III) from p-nitrobromoacetophenone by replacing the bromine by the acetoxy group, followed by hydrolysis of the not isolated acetyl derivative with boiling water. The acetyl derivative of p-nitrobenzoylcarbinol was obtained later by Bradley and Schwarzenbach by heating ω-diazo-p-nitroacetophenone with acetic acid [3]. They give a m. p. of 121-122° for the compound. We synthesized the acetyl derivative of carbinol (III) from p-nitrochloroacetophenone and also obtained a compound with m. p. 121-122°. Hydrolysis of this compound by refluxing with dilute sulfuric acid gave a compound with m. p. 132-133°, which failed to depress the melting point when mixed with the compound (III) obtained by the oxidation of p-nitrophenylethylene glycol. As a result, Engler and Zielke assumed that the acetyl derivative was (III).

The reduction of the m- and p-nitrophenylethylene glycols to the corresponding amino compounds was accomplished using hydrogen in the presence of either Raney nickel or platinum catalyst. We also obtained m-aminophenylchloromethylcarbinol by the reduction of the corresponding nitro compound with hydrogen in the presence of platinum.

The reduction of p-nitrophenylchloromethylcarbinol in alcohol solution with hydrogen, either when heated in the presence of Raney nickel, or when run in the cold in the presence of platinum, yields high-melting products of unestablished structure. We were able to obtain the acetyl derivative of p-aminophenylchloromethylcarbinol by reduction of the nitro compound with hydrogen in a mixture of acetic acid and acetic anhydride as the solvent, and using platinum as the catalyst. All of the obtained amino compounds were converted to the corresponding azo dyes by coupling with β-hydroxynaphthoic acid.

EXPERIMENTAL

p-Nitrophenylethylene glycol. a) A mixture of 40 g of p-nitrophenylchloromethylcarbinol (m. p. 84°), 20 g of potassium carbonate and 80 ml of water was heated with constant stirring at 100° for 35 hours. The mixture was cooled and then extracted in a liquid extractor with dichloroethane for 15 hours. The dichloroethane layer was dried, and the dichloroethane was removed by distillation. Yield 36.2 g (61.6%), m. p. 79-80°. For analysis the compound was recrystallized from chloroform. M. p. 81-82°. The compound is readily soluble in water, alcohol and acetone, and more difficultly soluble in chloroform and benzene.

Found %: N 7.56, 7.63. $C_8H_9O_4N$. Calculated %: N 7.65.

b) A mixture of 5 g of p-nitrostyrene oxide and 50 ml of 1% sulfuric acid was stirred for 24 hours at 50°. A small amount of oil layer was separated. One gram of barium chloride was added to the water solution. The barium sulfate was filtered, and the water was vacuum-distilled on the water bath. The product solidified on cooling and was recrystallized from dichloroethane. Yield 3.2 g (58%), m. p. 78-79°. The mixed melting point with the product obtained in (a) was not depressed.

The dibenzoyl derivative of p-nitrophenylethylene glycol was obtained by heating the glycol with benzoyl chloride in pyridine. M. p. 108-109° (from methyl alcohol).

Found %: N 3.74, 3.78. $C_{22}H_{17}O_6N$. Calculated %: N 3.58.

m-Nitrophenylethylene glycol was obtained in the same manner as the p-isomer by method (a): from 57.7 g of m-nitrophenylchloromethylcarbinol (m. p. 44°) we obtained 43.8 g (84%) of the glycol with m. p. 79°. For analysis the product was recrystallized from chloroform. M. p. 80°.

Found %: N 7.76, 7.84. $C_8H_9O_4N$. Calculated %: N 7.65.

The diacetyl derivative of m-nitrophenylethylene glycol was obtained by heating the latter with acetic anhydride in pyridine. M. p. 86-87° (from methanol).

Found %: N 5.21, 5.36. $C_{12}H_{13}O_6N$. Calculated %: N 5.24.

b) A mixture of 48.7 g of the acetyl derivative of m-nitrophenylchloromethylcarbinol with m. p. 72°, 22 g of potassium acetate and 50 ml of glacial acetic acid was refluxed for 10 hours. The mixture was then poured into water. The product was filtered and washed with water. The yield of the diacetyl derivative of m-nitrophenylethylene glycol was 43.1 g (80.7%), m. p. 84-85°. After recrystallization from methanol, m. p. 86-87°. The mixed melting point with the product obtained from m-nitrophenylethylene glycol was not depressed. A mixture of 24.5 g of the diacetyl derivative and 25 ml of 10% sulfuric acid was refluxed for 4 hours; the solution after cooling was neutralized with 17 ml of 40% NaOH solution, the mixture extracted with ether, the ether solution dried, the ether distilled off, and the residue allowed to crystallize. Yield 16.4 g (97.5%), m. p. 77°. The mixed melting point with the glycol obtained by method (a) was not depressed.

p-Nitrobenzoylcarbinol. a) A mixture of 10 g of p-nitrophenylethylene glycol and 15 ml of nitric acid (d 1.35) was allowed to stand at 20° for 48 hours. The mixture was then diluted with water. The precipitate was filtered, washed, and dried. Yield 5.5 g (55.5%), m. p. 133-134°. After recrystallization from water, m. p. 134-135°.

Found %: N 7.60, 7.68. $C_8H_7O_4N$. Calculated %: N 7.78.

b) A mixture of 20 g of p-nitrochloroacetophenone (m. p. 91-92°), 12 g of potassium acetate and 20 ml of acetic acid was refluxed for 2 hours. The mixture was then diluted with water. The precipitate was filtered and recrystallized from methanol. Yield 17 g (75.5%), m. p. 121-122°.

A mixture of 5 g of p-nitrobenzoylcarbinol acetate and 125 ml of 5% sulfuric acid was refluxed for 30 minutes. The mixture was then cooled and the obtained precipitate was recrystallized from water; m. p. 132-133°. The material failed to depress the melting point when mixed with the compound obtained by method (a).

p-Aminophenylethylene glycol. a) To a solution of 1.8 g of p-nitrophenylethylene glycol in 20 ml of water was added 0.5 g of Raney nickel and then the hydrogenation was run at 70-80°. The catalyst was filtered, and the water was distilled using the vacuum of the water-jet pump. The product was recrystallized from benzene. Yield 1 g (66%). M. p. 98-99°.

Found %: N 8.99, 9.23. $C_8H_{11}O_2N$. Calculated %: N 9.15.

b) To a solution of 3 g of p-nitrophenylethylene glycol in 15 ml of alcohol was added 0.05 g of platinum catalyst and then the hydrogenation was run at room temperature with shaking on a mechanical shaker. The catalyst was filtered, and the alcohol was vacuum-distilled. Yield 2.4 g (97%). M. p. 98-99°.

m-Aminophenylethylene glycol was obtained in the same manner as the p-isomer and in the same yields. M. p. 68-69° (from chloroform).

Found %: N 8.86, 8.88. $C_8H_{11}O_2N$. Calculated %: N 9.15.

Acetyl derivative of p-aminophenylchloromethylcarbinol. To a solution of 3 g of p-nitrophenylchloromethylcarbinol in a mixture of 10 ml of acetic anhydride and 5 ml of glacial acetic acid was added 0.05 g of platinum catalyst and the hydrogenation run at room temperature with shaking on a mechanical shaker. The catalyst was filtered. The filtrate was diluted with cold water. The product was recrystallized from aqueous alcohol. The yield was quantitative. M. p. 132-133°.

Found %: N 6.22, 6.25. $C_{10}H_{12}O_2NCl$. Calculated %: N 6.55.

m-Aminophenylchloromethylcarbinol. A solution of 3 g of m-nitrophenylchloromethylcarbinol in 15 ml of alcohol was hydrogenated in the presence of platinum catalyst (0.05 g). The yield was quantitative (2.4 g). M. p. 72-73° (from benzene).

Found %: N 7.88, 8.09. $C_8H_{10}ONCl$. Calculated %: N 8.15.

Dyes were obtained when the above amino compounds were diazotized and then coupled with β-hydroxynaphthoic acid. The dye from p-aminophenylethylene glycol was obtained as red needles (IV) with m. p. 224-225°, and λ_{max} 515 mμ; the dye from m-aminophenylethylene glycol was obtained as red-violet needles (V) with m. p. 215-216°, and λ_{max} 509 mμ; the dye from m-aminophenylchloromethylcarbinol was obtained as red needles (VI) with m. p. 223-224°, and λ_{max} 509 mμ.

Analysis IV. Found %: N 7.78, 7.85. $C_{19}H_{16}O_5N_2$. Calculated %: N 7.95.

Analysis V. Found %: N 8.18, 8.26. $C_{19}H_{16}O_5N_2$. Calculated %: N 7.95.

Analysis VI. Found %: N 7.82, 7.83. $C_{19}H_{15}O_4N_2Cl$. Calculated %: N 7.55.

SUMMARY

The following compounds were synthesized: m- and p-nitrophenylethylene glycols, m- and p-aminophenylethylene glycols, p-nitrobenzoylcarbinol, m-aminophenylchloromethylcarbinol, and p-acetamidophenylchloromethylcarbinol.

LITERATURE CITED

1. L. M. Yagupol'skii, B. E. Gruz, and A. I. Kiprianov, Zhur. Obshch. Khim. 28, 1608 (1958).*
2. C. Engler and O. Zielke, Ber. 22, 204 (1889).
3. W. Bradley and G. Schwarzenbach, J. Chem. Soc. (1928), p. 2907.

* Original Russian pagination. See C. B. translation.

1-PHENYL-2-TRIFLUOROMETHYLETHYLENE, PHENYLTRIFLUORO-METHYLACETYLENE, AND THEIR DERIVATIVES

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The purpose of the present investigation was to synthesize the vinylene homolog of benzotrifluoride (I) and the corresponding acetylenic compound (II).

$C_6H_5CH{=}CH{-}CF_3$ (I) $C_6H_5C{\equiv}C{-}CF_3$ (II)

As the starting compound we took 1-phenyl-2-trichloromethylethylene (III), obtained by the addition of trichlorobromomethane to styrene and subsequent cleavage of hydrogen bromide [1, 2].

It is known that the chlorine in benzotrichloride is easily replaced by fluorine using antimony trifluoride without a catalyst [3]. It was interesting to determine if a similar exchange would take place in the vinylene homolog of benzotrichloride. It proved that tarring occurs when (III) is heated with antimony trifluoride, either in the presence or absence of antimony pentachloride. The fluorination of (III) in dichloroethane solution leads to a mixture of chlorofluoro derivatives. The obtained product is difficult to separate from the solvent if the reaction is run in chlorobenzene. Using antimony trifluoride, replacement of the chlorine in compound (III) by fluorine goes smoothly in dioxane solution. Here (I) is obtained in good yield.

1-Phenyl-2-trifluoromethylethylene (I) is a colorless liquid with a pleasant odor, and is readily soluble in all organic solvents. It readily adds chlorine or bromine to yield a mixture of two diastereomers. It proved impossible to separate them by vacuum-distillation. A pure isomer was isolated when the solid dibromide was recrystallized until the melting point remained constant. This isomer was heated with concentrated sulfuric acid to convert it to the corresponding dibromocinnamic acid. However, decomposition of the compound occurred here with the formation of tar and the evolution of CO_2, HBr, Br_2 and HF. We were also unable to hydrolyze phenyltrifluoromethylethylene to the cinnamic acid by heating with concentrated sulfuric acid. Here the reaction went with the formation of polystyrene.

1-Phenyl-2-trifluoromethylethylene does not enter into dienic synthesis. The formation of an adduct fails to occur when the compound is heated with anthracene in refluxing xylene for 24 hours, or when it is heated with cyclopentadiene in benzene solution in a sealed ampul for 3 hours at 90° and for 2 hours at 130°. (I) does not give the oxide when reacted with benzene hydroperoxide by the Prilezhaev method, in chloroform solution at 20° for 4 days, and does not add trichlorobromomethane when refluxed in the presence of benzoyl peroxide for 12 hours.

(II) was obtained according to the scheme:

$$C_6H_5CH(Br)-CHBrCF_3 \xrightarrow{N(C_2H_5)_3} C_6H_5CH{=}CBrCF_3 \xrightarrow{KOH} (II)$$
(IV) (V)

Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Analysis results (in %) (the calculated values are given in parentheses)		
				Found	Calculated			
$C_6H_5CH{=}CH{-}CF_3$	165—166° (760)	1.1793	1.4750	41.110	39.385	1.725	C 62.68, 62.93 (62.75)	H 4.07, 4.10 (4.07)	F 33.35, 33.47 (33.11)
	114—115 (150)								
	61—62 (20)								
$C_6H_5C{\equiv}C{-}CF_3$	144—145 (760)	1.1509	1.4615	40.287	37.788	2.499	C 63.35, 63.37 (63.53)	H 2.96, 3.03 (2.97)	F 33.40, 33.79 (33.50)
	63—64 (45)								
$C_6H_5CHClCHClCF_3$	90—91 (15)	1.3979	1.4850	49.837	49.586	0.251	C 44.58, 44.72 (44.46)	H 2.87, 3.04 (2.91)	Cl 29.24, 29.40 (29.18)
$C_6H_5CH{=}C{-}CF_3$	194—195 (760)	1.5362	1.5141	49.216	47.150	2.066	C 43.23, 43.25 (43.05)	H 2.40, 2.44 (2.41)	Br 31.75, 31.76 (31.83)
$\quad\quad\quad

and then it was washed with water, 5% sodium carbonate solution, and again with water. The solution was dried, the ether was distilled off, and the residue was vacuum-distilled. The fraction with b. p. 60-62° at 20 mm was collected. For purification, the product was redistilled. Yield 83 g (80%).

1-Phenyl-1,2-dibromo-3,3,3-trifluoropropane (IV). To a solution of 13 g of (I) in 40 ml of dry chloroform was added 3.9 ml of bromine and the mixture was heated for 1 hour at 40-50°, with illumination by a 300-watt lamp. When the solution had decolorized, the chloroform was vacuum-distilled using a water-jet pump. The yield of the dibromide was quantitative (24.8 g). The mixture was vacuum-distilled, b. p. 86-89° at 0.1 mm.

Found %: C 32.50, 32.52; H 1.93, 1.97; Br 48.05, 48.20. $C_9H_7Br_2F_3$. Calculated %: C 32.56; H 2.13; Br 48.14.

Recrystallization of the mixture from aqueous methanol gave one of the isomers in 64% yield. M. p. 59.5°.

Found %: Br 48.37, 48.56. $C_9H_7Br_2F_3$. Calculated %: Br 48.14.

1-Phenyl-1,2-dichloro-3,3,3-trifluoropropane. To a solution of 4.33 g (0.025 mole) of (I) in 10 ml of dry carbon tetrachloride was added a solution of 2.22 g (0.0315 mole) of chlorine in 30 ml of carbon tetrachloride and the mixture heated for 1 hour at 60°, with illumination by a 300-watt lamp. The solvent was removed by distillation through a Vigreux column, while the residue was vacuum-distilled. The fraction with b. p. 90-91° at 15 mm was collected. For analysis, the product was redistilled. Yield 4.3 g (92%).

1-Phenyl-2-bromo-2-trifluoromethylethylene (V). A mixture of 13.3 g of (IV) and 90 ml of dry triethylamine was refluxed with stirring for 6 hours, cooled, and the crystals of triethylamine hydrobromide filtered. The filtrate was poured into 0.5 liter of 10% sulfuric acid and the product was extracted with ether (2 x 150 ml). The combined ether extract was washed with 10% sulfuric acid, water, 5% sodium carbonate solution, again with water, and dried. The ether was distilled off. The product was vacuum-distilled. Yield 7.85 g (90%).

Phenyltrifluoromethylacetylene (II). A charge of 20 g of KOH was placed in a Claisen flask and heated in an oil bath at 230° (bath temperature). Then 12.6 g of (V) was added from a dropping funnel at a rate of 1 drop every 1-2 seconds. The bath temperature was raised as (V) was added, and at the end of addition was 250°. The flask contents were shaken at periodic intervals. Then (II) was steam-distilled. The steam distillate was extracted with ether, the water was separated, and the ether solution was dried. The ether was distilled off, and the product was distilled through a 10 cm Vigreux column. The first fraction was collected up to 145°, while the second fraction had b. p. 145-165°. The 2nd fraction was treated once more with KOH, as described above. The total yield of phenyltrifluoromethylacetylene with b. p. 144-145° was 6.45 g (76%).

1-Phenyl-1,2-dibromo-2-trifluoromethylethylene. To a solution of 2.55 g of (II) in 10 ml of dry chloroform was added 0.8 ml of bromine. The mixture was heated for 1 hour at 40-50°, with illumination by a 300-watt lamp. When decolorization occurred the chloroform was distilled through a Vigreux column. The residue was vacuum-distilled. Yield 4.3 g (87%).

1-Phenyl-1,1,2,2-tetrachloro-3,3,3-trifluoropropane. To a solution of 3.4 g (0.02 mole) of (II) in 5 ml of dry carbon tetrachloride was added a solution of 3.4 g of chlorine (0.048 mole) in 30 ml of carbon tetrachloride. The mixture was illuminated and heated for 1 hour at 50-60°, and then refluxed for 15 minutes. When the solution had decolorized, the carbon tetrachloride was distilled off. The residue was vacuum-distilled. Yield 5.35 g (86%).

SUMMARY

1-Phenyl-2-trifluoromethylethylene, phenyltrifluoromethylacetylene, and their halo derivatives were synthesized, and a study made of their properties.

LITERATURE CITED

1. M. S. Kharasch, E. V. Jensen, and W. H. Urry, J. Am. Chem. Soc. 69, 1100, 1105 (1947).
2. A. N. Nesmeyanov, R. Kh. Freidlina, L. I. Zakharkin, and A. B. Belyavskii, Zhur. Obshch. Khim. 26, 1070 (1956).*

* Original Russian pagination. See C. B. translation.

3. F. Swarts, Bull. acad. Roy. Belg. (1920), p. 389; Chem. Zentr. III, 32 (1921); Chem. Abs. 16, 2316 (1922).
4. A. L. Henne and J. B. Hinkamp, J. Am. Chem. Soc. 67, 1194 (1945).
5. A. Blomquist and D. Longone, J. Am. Chem. Soc. 79, 4981 (1957).
6. A. L. Henne, J. V. Schmitz, and W. G. Finnegan, J. Am. Chem. Soc. 72, 4195 (1950).
7. R. N. Haszeldine, J. Chem. Soc. (1953), p. 3371.
8. A. Henne and M. Nager, J. Am. Chem. Soc. 73, 1042 (1951).
9. P. Grammaticakis and T. Chauvelier, Compt. rend. 238, 1232 (1954); Chem. Zentr. (1954), p. 9246; Chem. Abs. 48, 8043c (1954).

PHENYLBIS(TRICHLOROMETHYL)PHOSPHINE OXIDE, PHENYLTRICHLOROMETHYLPHOSPHINIC ACID, AND THEIR DERIVATIVES

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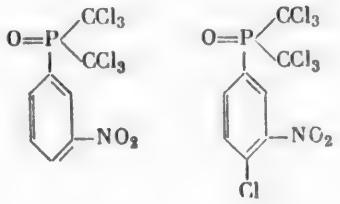
The purpose of the present investigation was to synthesize some compounds in which the phosphorus atom is linked to the benzene ring and to either one or two trichloromethyl groups. As the starting compound we took ω,ω'-dichlorodimethylphenylphosphine oxide [1]. This compound was chlorinated at 150-215° to give phenylbis(trichloromethyl)phosphine oxide (I).

$$C_6H_5\overset{\overset{O}{\|}}{P}(CH_2Cl)_2 \longrightarrow C_6H_5\overset{\overset{O}{\|}}{P}(CCl_3)_2$$
(I)

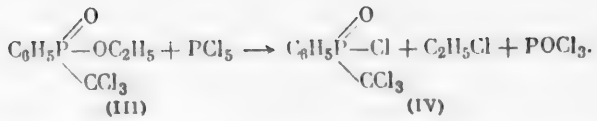
We also obtained ω,ω'-dichlorodimethyl(p-chlorophenyl)phosphine oxide by reacting p-chlorophenylphosphorus tetrachloride with diazomethane, and then by chlorination converted it to p-chlorophenylbis(trichloromethyl)phosphine oxide (II).

Oxides (I) and (II) are colorless crystalline compounds that are not affected by aqueous solutions of acids or alkalies either in the cold or when heated up to 100°. In contrast to benzotrichloride, phenyl trichloromethyl ether and phenyl trichloromethyl sulfide, the arylbis(trichloromethyl)phosphine oxides (I and II) are so stable that we were able to nitrate them with mixed acid at 100°. Here the nitro derivatives with the following structure were obtained.



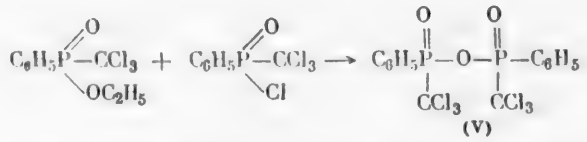
There is no doubt as to the position of the nitro groups, since it was shown by us that ω,ω'-dichlorodimethylphenylphosphine oxide nitrates exclusively in the meta-position [1].

As the starting compound for the synthesis of the derivatives of phenyltrichloromethylphosphinic acid we took the ethyl ester of the acid. The latter was obtained from the ethyl ester of phenylphosphinous acid and carbon tetrachloride by the G. Kamai method [2]. We investigated the reaction of ethyl phenyltrichloromethylphosphinate (III) with PCl_5. The heating of (III) with 1 mole of PCl_5 at 110-120° yields phenyltrichloromethylphosphinic chloride (IV) according to the equation:



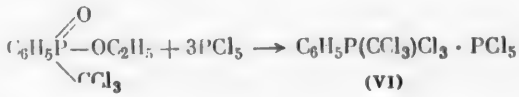
(III) (IV)

The amount of ethyl chloride and phosphorus oxychloride evolved in this reaction does not exceed 75% of the theoretical even when the mixture is heated to 140-160°. Besides chloride (IV), a certain amount of phenyltrichloromethylphosphinic anhydride (V) is always formed, apparently according to the scheme:



(V)

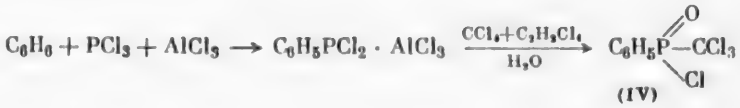
That it is possible for anhydride (V) to be formed in this reaction was confirmed by special experiment. It proved that the reaction of ester (III) with 2 moles of PCl_5 also failed to give the pure chloride (IV), devoid of the phenyltrichloromethylphosphinic anhydride as impurity. Complex (VI) is formed when ester (III) is heated with 3 moles of PCl_5 at 100-120°, and then at 160°.



(VI)

Hydrolysis of this complex yields phenyltrichloromethylphosphinic chloride (IV) in quantitative yield.

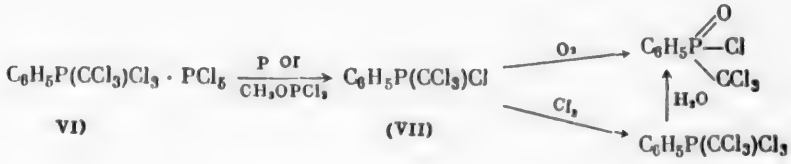
After the present investigation had been completed, we learned of a reference [3] where the following scheme is given for obtaining chloride (IV):



(IV)

We repeated this synthesis, replacing the tetrachloroethane by an excess of CCl_4, which served simultaneously as reagent and solvent, and obtained chloride (IV) in 54% yield.

A. V. Kirsanov and G. K. Fedorova found that complexes of composition $ArPCl_3 \cdot PCl_5$ are formed when arylphosphinic chlorides are heated with 2 moles of PCl_5. In a similar manner, the heating of phenyltrichloromethylphosphinic chloride with 2 moles of PCl_5 gives complex (VI). The reduction of (VI) with red phosphorus, or even better by the method of [4] with methyl phosphorodichloridite, yields phenyltrichloromethylphosphorus chloride (VII).



(VI) (VII)

(VII) oxidizes in the air with the evolution of heat; it adds 1 mole of chlorine, and hydrolysis of the chlorination product yields the same compound as is obtained by oxidation, namely phenyltrichloromethylphosphinic chloride.

EXPERIMENTAL

ω,ω'-Dichlorodimethylphenylphosphine oxide had m. p. 141-142° [1].

ω,ω'-Dichlorodimethyl(p-chlorophenyl)phosphine oxide was synthesized in the same manner as the previous compound. From 0.1 mole of p-chlorophenylphosphorus tetrachloride and 0.23 mole of diazomethane, after hydrolysis with water, we obtained 10.8 g (42%) of the compound, m. p. 150-151° (from aqueous methyl alcohol or from benzene).

Found %: Cl 40.86, 40.97. $C_8H_8OPCl_3$. Calculated %: Cl 41.36.

Phenylbis(trichloromethyl)phosphine oxide (I). Into a flask, fitted with an inlet tube for chlorine and a reflux air condenser connected to a calcium chloride tube, was charged 6.7 g of ω,ω'-dichlorodimethylphenylphosphine oxide. The compound was heated to 150° and then a slow stream of dry chlorine was passed into the melt. The chlorination was run at 150 to 215° for 28-30 hours until the calculated weight increase (4.14 g) was obtained. At the end of chlorination the compound crystallized on cooling. The compound was obtained as colorless crystals when recrystallized from either alcohol or a mixture of benzene and ligroin. Yield 7 g (64.5%), m. p. 133-134°. The compound is very soluble in benzene, and is insoluble in petroleum ether.

Found %: Cl 58.86, 59.14. $C_8H_5OPCl_6$. Calculated %: Cl 59.0.

p-Chlorophenylbis(trichloromethyl)phosphine oxide (II) was obtained in the same manner as the preceding compound. ω,ω'-Dichlorodimethyl(p-chlorophenyl)phosphine oxide (3.8 g) was chlorinated at 170-220° for 19 hours. Yield 3.25 g (57%), m. p. 148-149° (from methyl alcohol or a mixture of benzene and ligroin).

Found %: Cl 63.13, 63.17. $C_8H_4OPCl_7$. Calculated %: Cl 62.83.

3-Nitrophenylbis(trichloromethyl)phosphine oxide. In a flask with ground-glass connection and fitted with a reflux condenser was placed a nitration mixture composed of 1.9 g of HNO_3 (d 1.5) and 2.9 g of H_2SO_4 (d 1.83), the mixture cooled to 0°, and then 1.8 g of phenylbis(trichloromethyl)phosphine oxide was added gradually with stirring. After this the mixture was heated on the boiling water bath for 45 minutes, then cooled, poured over ice, and the product filtered and washed with water. Yield 1.9 g (93.6%); pale yellow crystals with m. p. 158-159° (from methyl alcohol or a mixture of ligroin and benzene).

Found %: Cl 52.33, 52.44; N 3.66, 3.78. $C_8H_4O_2NPCl_6$. Calculated %: Cl 52.46; N 3.45.

3-Nitro-4-chlorophenylbis(trichloromethyl)phosphine oxide. A mixture of 1.2 g of p-chlorophenylbis(trichloromethyl)phosphine oxide and a nitration mixture composed of 1.2 g of HNO_3 (d 1.5) and 1.8 g of H_2SO_4 (d 1.83) was heated for 1.5 hours on the boiling water bath. Yield 1.1 g (85%). After recrystallization from ligroin, m. p. 172-173°.

Found %: Cl 56.25, 56.29; N 3.46, 3.47. $C_8H_3O_2NPCl_7$. Calculated %: Cl 56.45; N 3.18.

The ethyl phenyltrichloromethylphosphinate (III) used in our work had m. p. 83-84° (from CCl_4) [2].

Phenyltrichloromethylphosphinic chloride (IV). a) In a flask with ground-glass connection was placed a mixture of 8.6 g (0.03 mole) of ethyl phenyltrichloromethylphosphinate and 18.8 g (0.09 mole) of PCl_5. The flask was connected to a descending condenser with receiver, which was protected by a calcium chloride tube. The mixture was heated for 2 hours in an oil bath at 110-120°. Toward the end of the second hour the mass became liquid. Then it was heated for 1 hour at 160°. Here the product solidified due to formation of the complex. The C_2H_5Cl and $POCl_3$ formed during reaction were collected in the receiver. At the end of reaction they were removed completely by distillation using the vacuum of a water-jet pump. The reaction mixture was then cooled and slowly hydrolyzed by the addition of water. After 4 hours the product was filtered, washed with water, and dried. Yield 8.3 g (99%), m. p. 87°. The melting point is not changed by recrystallization of the compound from dry CCl_4. The compound is readily soluble in alcohol, benzene, chloroform, dichloroethane, and acetone.

Found %: Cl 50.87, 50.98. $C_7H_5OPCl_4$. Calculated %: Cl 51.2.

b) Into a reactor, fitted with a stirrer, dropping funnel, and a reflux condenser connected to a calcium chloride tube, were charged 41.2 g (0.3 mole) of distilled PCl_3, 13.3 g (0.1 mole) of $AlCl_3$, and 7.8 g (0.1 mole) of dry benzene. The mixture was heated under reflux in an oil bath with stirring. The excess PCl_3 was

vacuum-distilled at a bath temperature of 60° using a water-jet pump. Then the mixture was cooled to room temperature, 50 ml of dry carbon tetrachloride was added, the mixture refluxed for 1.5 hours, then cooled in an ice-salt mixture, and 13 ml of water added in 1 hour with vigorous stirring; then the cooling bath was removed and the mixture was stirred for another 3 hours. This was followed by filtration of the reaction mixture to remove aluminum hydroxide, which was washed with carbon tetrachloride, and then the combined filtrate was distilled to remove CCl_4 to incipient crystallization, at which point the residue was cooled; the obtained crystals were filtered, washed with a very small amount of CCl_4, and dried. Yield 15 g (54%), m. p. 85-86°. Recrystallization from dry CCl_4 gave 12.5 g (45% yield) of product with m. p. 87°. The mixed melting point with the product obtained by method (a) was not depressed.

The heating of phenyltrichloromethylphosphinic chloride with dilute nitric acid yields phenyltrichloromethylphosphinic acid with m. p. 163-164° [3].

Phenyltrichloromethylphosphinic anhydride (V). a) A mixture of 11.5 g (0.04 mole) of ethyl phenyltrichloromethylphosphinate and 8.5 g (0.0408 mole) of PCl_5 was heated in a glycerin bath at 100-120° for 2 hours. The ethyl chloride and part of the $POCl_3$ formed in the reaction distilled during this time. The remaining $POCl_3$ was removed by vacuum-distillation using a water-jet pump. The product was recrystallized from dry carbon tetrachloride. Yield 2.4 g (23.3%), m. p. 170-172°. White crystalline compound, readily soluble in hot chloroform, dichloroethane, carbon tetrachloride, and benzene.

Found %: Cl 42.53, 42.47. $C_{12}H_{10}O_3P_2Cl_6$. Calculated %: Cl 42.51.

Evaporation of the mother liquor gave a precipitate of phenyltrichloromethylphosphinic chloride with m. p. 83-85°.

b) A mixture of 2.8 g (0.01 mole) of phenyltrichloromethylphosphinic chloride in 12 ml of benzene, 1.1 g (0.014 mole) of pyridine and 0.1 g (0.005 mole) of water was refluxed for 3 hours. The mixture was cooled, filtered to remove pyridine hydrochloride, the benzene solution evaporated in vacuo to dryness, and the residue treated with water to give a white crystalline compound, which was filtered and then recrystallized from carbon tetrachloride, m. p. 169-171°. Yield 0.6 g (24%). The mixed melting point with the product obtained by method (a) was not depressed.

Complex of phenyltrichloromethylphosphorus trichloride with phosphorus pentachloride (VI). a) Into a flask, fitted with a reflux condenser (ground-glass connection), were charged 13.9 g (0.05 mole) of phenyltrichloromethylphosphinic chloride and 22.5 g (0.107 mole) of PCl_5, and the reactants mixed well. Then the mixture was heated for 4 hours in a glycerin bath at 150-160°. The reflux condenser was replaced by a descending condenser, connected to a receiver fitted with a calcium chloride tube. The $POCl_3$ was distilled off at 160°, at the end using the vacuum of a water-jet pump. The obtained solid product was refluxed with benzene. After settling, the benzene was decanted hot. This washing was repeated 3 to 4 times. The product was dried in a vacuum-oven to constant weight. Yield 15.5 g (57.4%), m. p. 202° (with decomposition, in a sealed capillary).

Found: equiv. (after hydrolysis) 8.75, 8.87. $C_7H_5P_2Cl_{11}$. Calculated: equiv. 9.

The starting compound was isolated from the benzene mother liquor. The benzene was vacuum-distilled, and the residue was cautiously decomposed with water using strong cooling. After several hours the phenyltrichloromethylphosphinic chloride was filtered (5 g).

Phenyltrichloromethylphosphorus chloride (VII). Into a flask with ground-glass connection, fitted with a dropping funnel, tube for the admittance of an inert gas, and a reflux condenser, was charged 27 g (0.05 mole) of complex (VI). The reaction was run in a stream of dry nitrogen. The flask was heated in a glycerin bath for 2 hours at 95-100°, and during this time 15 g (0.113 mole) of methyl phosphorodichloridite was added in drops. At the end of addition the mixture was heated at the same temperature for another 30 minutes. The product was vacuum-distilled in a stream of nitrogen. Yield 10.3 g (78.4%). B. p. 112-114° at 3 mm. Colorless liquid with a very pungent odor. The compound oxidizes easily in the air with the evolution of heat.

Found %: P 12.11, 12.17. $C_7H_5PCl_4$. Calculated %: P 11.83.

A charge of 1.3 g of freshly distilled phenyltrichloromethylphosphorus chloride was placed in a flask and then a stream of dry chlorine was passed into it, with periodic cooling of the flask in cold water, until the

theoretical weight increase was obtained. We obtained 1.66 g (100% yield) of crystalline phenyltrichloromethylphosphorus trichloride. After cautiously treating it with water, the compound was allowed to stand for several hours. Filtration gave 1.3 g (93.5% yield) of phenyltrichloromethylphosphinic chloride. M. p. 87°. The filtrate was transferred to a 500 ml volumetric flask and made up to volume. Then the equivalent was determined.

Found: equiv. (after hydrolysis) 2.02. $C_7H_5PCl_6$. Calculated: equiv. 2.0.

SUMMARY

Phenylbis(trichloromethyl)phosphine and p-chlorophenylbis(trichloromethyl)phosphine oxides were synthesized. Their nitration gave 3-nitrophenylbis(trichloromethyl)phosphine oxide and 3-nitro-4-chlorophenylbis(trichloromethyl)phosphine oxide, respectively. The synthesis of phenyltrichloromethylphosphinic chloride is described, as well as of the complex of phenyltrichloromethylphosphorus trichloride with phosphorus pentachloride, and of its reduction product – phenyltrichloromethylphosphorus chloride.

LITERATURE CITED

1. L. M. Yagupol'skii and P. A. Yufa, Zhur. Obshch. Khim. 28, 2853 (1958).*
2. G. Kamai, Zhur. Obshch. Khim. 18, 443 (1948).
3. P. Biddle, J. Kennedy, and J. L. Willans, Chem. and Ind. (London) (1957), p. 1481.
4. L. D. Quin and C. H. Rolston, J. Org. Chem. 23, 1693 (1958).

* Original Russian pagination. See C. B. translation.

SYNTHETIC DYES

XV. SYNTHESIS OF N-p-TOLYL-6-METHYLLEPIDINIUM IODIDE AND ITS TRANSFORMATIONS

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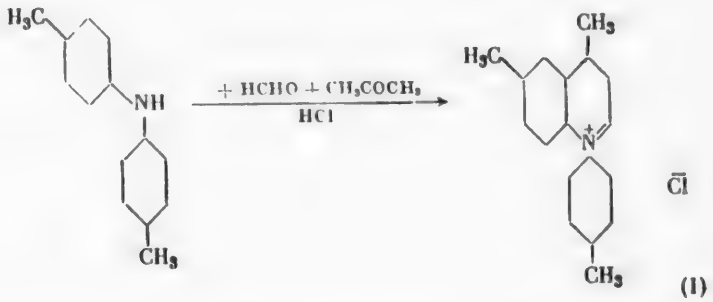
Earlier, we had shown that it is possible to effect the ortho-cyclization of both symmetrical and unsymmetrical secondary aromatic amines with paraldehyde, acetaldehyde, formaldehyde, paraform, acetone and vinyl ethers to yield N-arylquinaldinium, -quinolinium and -lepidinium derivatives [1].

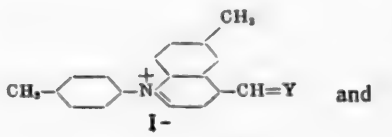
Expanding our investigations in this direction and applying the Beyer reaction [2] to secondary aromatic amines, we ran the reaction with p,p'-ditolylamine to yield the quaternary salt in accordance with the following scheme.



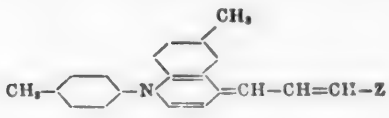
(I)

The obtained quaternary salt, 1-p-tolyl-6-methyllepidinium iodide (I), was used to obtain cyanine dyes (see table).

Dyes:

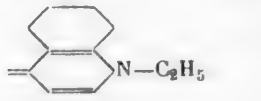
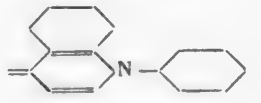
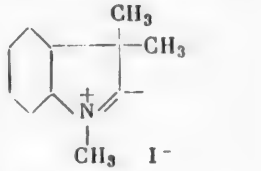
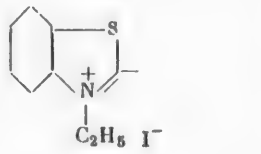


and



A comparison of the absorption maxima of the obtained dyes with those of the dyes synthesized from N-phenyllepidinium iodide is given in the table. From this it follows that introducing a methyl group in the 6-position to the phenyl group of the radical causes a bathochromic shift of the absorption maximum by 4-6 mμ.

In the case of styryl the shift takes place in the short-wave portion of the spectrum to the extent of 8 mμ. When the indicated dyes are compared with the analogous isomers, obtained from the 1-p-tolyl-6-methylquinaldinium salt, we observe a strong bathochromic shift (50-58 mμ) of the absorption maximum, which is due to an elongation of the principal chromophore on the vinylene group inside the ring and to an increase in the energy level at the moment of excitation of the molecule. The absorption curves are shown in the figure.

Compound No.	Value of Y and Z	Absorption maxima of the dyes (in mμ)		
		As shown by the formulas	No CH_3 groups in 6 and para-positions	Isomeric with those obtained (synthesized from quinaldium salt)
II	Y	571	579	—
III	 Y	597	593	—
IV	 Y	607	602	—
V	 Z	622	618	572
VI	 Z	646	640	588

EXPERIMENTAL

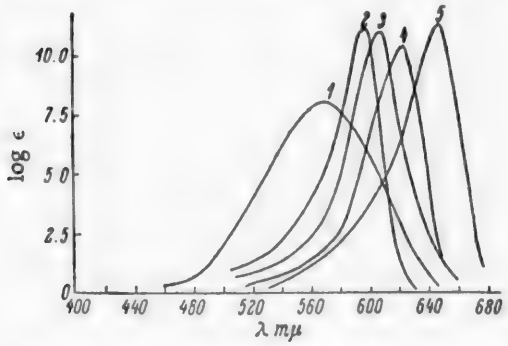
1-p-Tolyl-6-methyllepidinium iodide (I). A mixture of 6 g of p,p'-ditolylamine and 1 g of dry paraform was ground well in a mortar to a homogeneous mass, after which it was transferred to a glass tube, followed by the addition of 10 ml of dioxane, 3 ml of hydrochloric acid (d 1.19) and 2.2 ml of acetone. The tube was sealed and heated for 6 hours on the boiling water bath. The reaction mass was obtained as a viscous liquid. The tube contents were repeatedly extracted with ether (until the ether was no longer colored), after which the somewhat tarry mass was dissolved in aqueous alcohol, and then aqueous potassium iodide solution was added until a precipitate ceased to form. The quaternary salt was filtered and recrystallized from aqueous alcohol. M. p. 135-136°; yield 4 g (35%). The salt is readily soluble in hot water, alcohol, pyridine, and chloroform, and practically insoluble in ether.

Found %: I 33.62, 33.74. $C_{18}H_{18}NI$. Calculated %: I 33.85.

(1-p-Tolyl-6-methyl-4-quinoline)-p-dimethylaminostyryl iodide (II) [3]. The dye was obtained by heating a mixture of 1.5 g of (I), 0.6 g of p-dimethylaminobenzaldehyde and 5 ml of pyridine in an oil bath for 30 minutes at gentle boil of the reaction mixture. The reaction product was extracted several times with ether. The dye, obtained as a powder, was recrystallized from aqueous alcohol. The dye was obtained as bronze-colored needlelike crystals with m. p. 170-172°. The absorption maximum of the dye lies at 571 mμ. Yield 1 g (60%).

Found %: I 25.28, 25.12. $C_{27}H_{27}N_2I$. Calculated %: I 25.06.

(1-p-Tolyl-6-methyl-4-quinoline) (1'-ethyl-4'-quinoline)-monomethinecyanine iodide (III) [4]. A mixture of 1 g of (I) and 2 g of quinoline ethiodide was dissolved in 25 ml of hot anhydrous ethyl alcohol. Then 2 ml of alcoholic KOH solution (10%) was added in drops to the hot solution and the mixture heated at gentle reflux for 15 minutes. Toward the end of heating the reaction mass assumed an intense blue-violet color. The next day the reaction product was transferred to a porcelain dish, the alcohol was evaporated on the water bath, and the residual tarry mass was digested several times with a small amount of water (until the water extract was neutral to litmus). The dye was precipitated with ether and then recrystallized from aqueous alcohol. The dark purple crystals of the dye melted at 202-203° (decomp.). Yield 1 g (40%). The absorption maximum of the compound in ethanol lies at 597 mμ.



Absorption curves of dyes. 1) (1-p-Tolyl-6-methyl-4-quinoline)-p-dimethylaminostyryl iodide (II); 2) (1-p-tolyl-6-methyl-4-quinoline)-(1-ethyl-4-quinoline) monomethinecyanine iodide (III); 3) (1-p-tolyl-6-methyl-4-quinoline) (1-phenyl-4-quinoline) monomethinecyanine iodide (IV); 4) (1-p-tolyl-6-methyl-4-quinoline)-(1,3,3-trimethyl-2-indolenine) trimethinecyanine iodide (V); 5) (1-p-tolyl-6-methyl-4-quinoline) (3-ethyl-2-benzothiazole)-trimethinecyanine iodide (VI).

Found %: I 24.58, 24.28. $C_{29}H_{27}N_2I$. Calculated Calculated %: I 24.30.

(1-p-Tolyl-6-methyl-4-quinoline) (1'-phenyl-4'-quinoline)-monomethinecyanine iodide (IV). The dye was obtained in the same manner as the preceding from 1 g of (I) and 2 g of N-phenylquinolinium iodide. After recrystallization from aqueous alcohol the dye had m. p. 195-197° (decomp.). Yield 1.2 g (42%). The absorption maximum of the compound in ethanol lies at 607 mμ.

Found %: I 22.49, 22.56. $C_{33}H_{27}N_2I$. Calculated %: I 22.62.

(1-p-Tolyl-6-methyl-4-quinoline) (1',3',3'-trimethyl-2-indolenine)-trimethinecyanine iodide (V) [5]. A mixture of 1.5 g of (I), 1.5 g of 2-β-acetanilidovinyl-1,3,3-trimethylindolenine iodide and 10 ml of pyridine, contained in a small flask fitted with a reflux condenser, was heated in an oil bath for 30 minutes at gentle reflux. The solution gradually assumed a blue color. The reaction mixture was extracted several times with ether until the latter was no longer colored. The powdery dye was recrystallized from alcohol. The obtained dye had m. p. 197-200° (decomp.). Yield 0.85 g (28.3%). The absorption maximum of the dye in ethanol lies at 622 mμ.

Found %: I 22.79, 22.68. $C_{31}H_{31}N_2I$. Calculated %: I 22.76.

(1-p-Tolyl-6-methyl-4-quinoline) (3'-ethyl-2'-benzothiazole)-trimethinecyanine iodide (VI). A mixture of 1.2 g of (I), 1.4 g of 2-β-acetanilidovinyl-3-ethylbenzothiazole iodide and 10 ml of pyridine was heated in an oil bath for 45 minutes at gentle reflux of the reaction mass. The reaction mass after cooling was treated with ether to remove the pyridine, while the residual dye was recrystallized from alcohol. The dye was obtained as a dark brown, finely crystalline powder with m. p. 236-238° (decomp.). Yield 0.7 g (37.5%). The absorption maximum of the dye in ethanol lies at 646 mμ.

Found %: I 22.46, 22.54. $C_{29}H_{27}N_2SI$. Calculated %: I 22.60.

All of the obtained dyes are readily soluble in alcohol, acetone, and chloroform, difficultly soluble in water (except styryl), and practically insoluble in ether. The absorption curves of the dyes were taken in ethanol solution using an automatically recording SF-2M spectrophotometer.

SUMMARY

1. The reaction of p,p'-ditolylamine with acetone and paraform in the presence of hydrochloric acid in dioxane solution gave 1-p-tolyl-6-methyllepidinium iodide.

2. Using this quaternary salt we synthesized 5 new cyanine dyes of unsymmetrical structure, and studied their spectrophotometric properties in the visible portion of the spectrum.

LITERATURE CITED

1. G. T. Pilyugin and Z. Ya. Krainer, Author's Certificate No. 94,015 (USSR); Doklady Akad. Nauk SSSR 81, 609 (1951); G. T. Pilyugin and B. M. Gutsulyak, Author's Certificate Nos. 103,319 and 109,979 (USSR); G. T. Pilyugin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1952), pp. 353, 512, 520, 736.*
2. C. Beyer, J. Prakt. Chem. 33, 393 (1886).
3. L. G. S. Brooker, Rev. Modern Phys. 14, 275 (1942); L. G. S. Brooker, A. L. Skar, H. W. J. Cressman, and co-workers, J. Am. Chem. Soc. 67, 1875 (1945).
4. H. Decker, Ber. 24, 690 (1891); F. M. Hamer, J. Chem. Soc. (1939), p. 1008; A. Miethe and G. Book, Ber. 37, 2821 (1904).
5. T. Ogata, Chem. Zentr. (1932), Vol. II, p. 711; (1931), Vol. I, p. 3297; British Patent 344,409; U. S. Patent 2,071,898 (1937).

* Original Russian pagination. See C. B. translation.

SYNTHETIC DYES

XVI. SYNTHESIS OF HYDROXY- AND ALKOXY-SUBSTITUTED N-ARYLQUINALDINIUM QUATERNARY SALTS AND THEIR TRANSFORMATIONS

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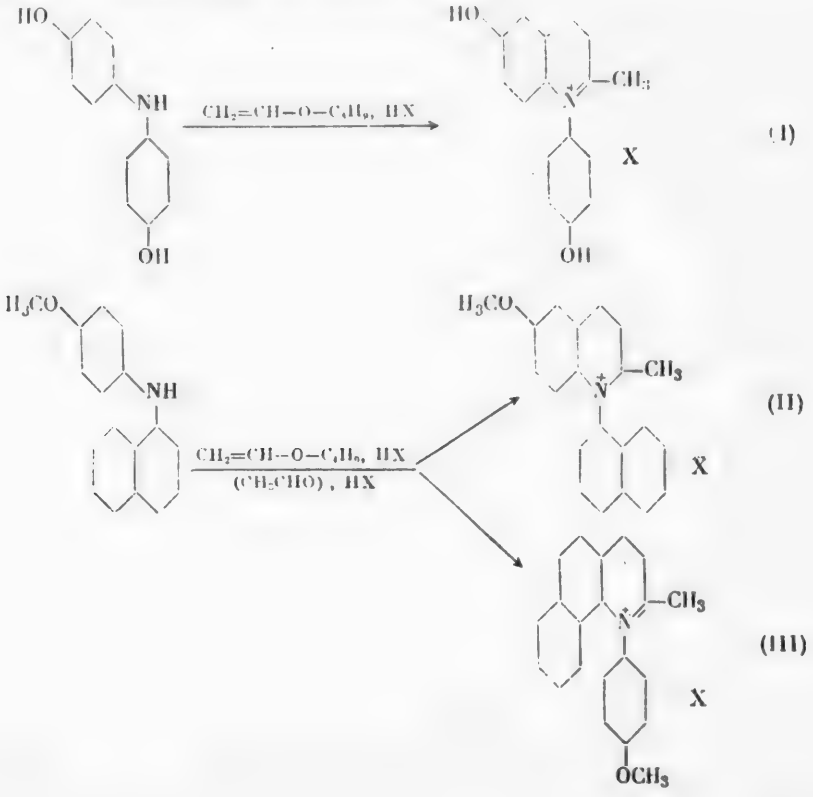
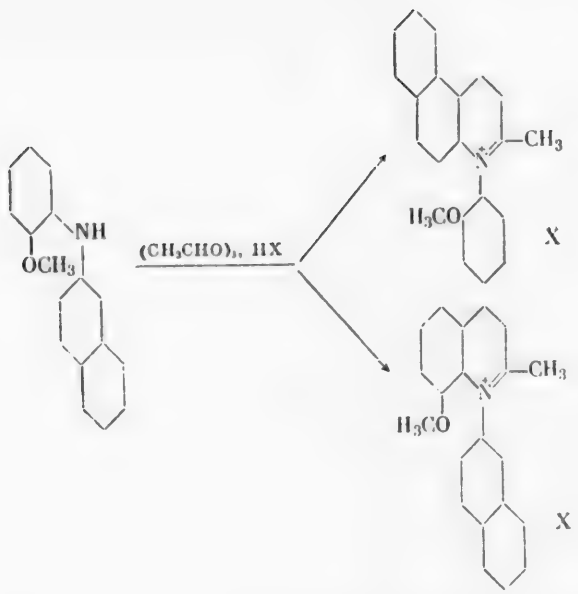
Earlier we had shown that the reaction of either symmetrical or unsymmetrical secondary aromatic amines with paraldehyde, acetaldehyde, vinyl ethers, formaldehyde, and acetone yields N-arylquinolinium, -quinaldinium and -lepidinium onium salts [1]. Different types of cyanine dyes were synthesized from these salts, the dyes were subjected to spectral analysis, and certain rules were established regarding the relationship between structure and the color of organic molecules [2].

As an expansion of these studies, we reacted p,p'-dihydroxydiphenylamine, p-methoxyphenyl-α-naphthylamine and o-methoxyphenyl-β-naphthylamine with paraldehyde and with vinyl n-butyl ether in acid medium. The reactions could go in accordance with the scheme [3]:





(IV)

(V)

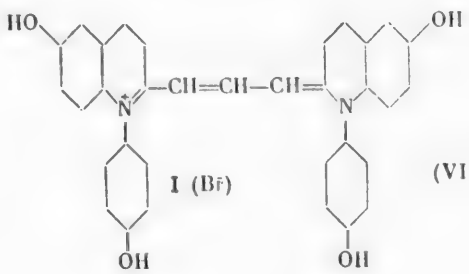
From this scheme it can be seen that the formation of isomeric salts is possible when unsymmetrical amines are taken for the condensation.

As a result of our investigation we isolated and studied the following salts: 1-p-hydroxyphenyl-6-hydroxyquinaldinium (I), 1-α-naphthyl-6-methoxyquinaldinium (II), and 1-o-methoxyphenyl-5,6-benzoquinaldinium (IV). We were unable to detect the presence of other compounds. The structure of the obtained salts was supported by the analytical data and by the absorption spectra of the symmetrical carbocyanines obtained from them, in which connection the carbocyanines showed slight bathochromic shifts of the absorption maxima when compared with the maxima of the analogous unsubstituted dyes.

p,p'-Dihydroxydiphenylamine was condensed with vinyl butyl ether, and the quaternary salt was isolated as the iodide in 20% yield, and as the bromide in 38% yield; p-methoxyphenyl-α-naphthylamine was condensed with vinyl butyl ether and with paraldehyde, in which connection better yields of the salt (40%) are obtained with the vinyl ether, while with paraldehyde they do not exceed 30%. The quaternary salt of this amine was obtained both as the iodide and as the perchlorate.

The following symmetrical carbocyanine dyes were synthesized by condensing the quaternary salts with orthoformic ester [4, 5]:

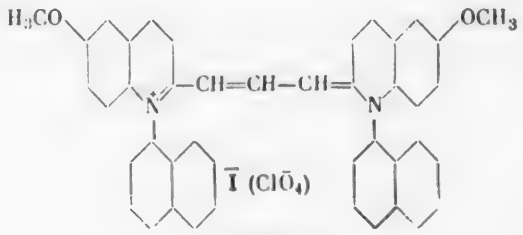
a) bis(1-p-hydroxyphenyl-6-hydroxy-2-quinoline)trimethinecyanine iodide (VI), with an absorption maximum in ethanol at 638 mμ;



(VI, VII)

b) bis(1-p-hydroxyphenyl-6-hydroxy-2-quinoline)trimethinecyanine bromide (VII), with an absorption maximum in ethanol at 637 mμ;

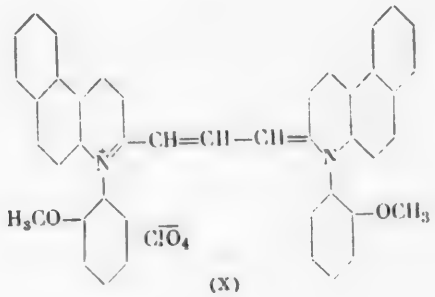
c) bis(1-α-naphthyl-6-methoxy-2-quinoline)trimethinecyanine iodide (VIII), with an absorption maximum at 635 mμ;



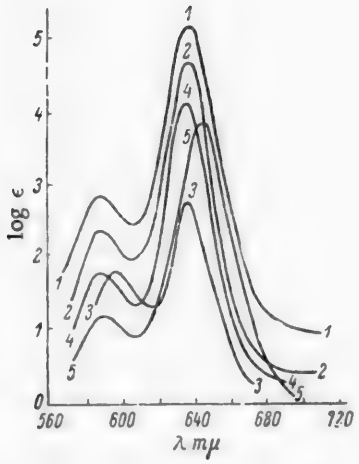
(VIII, IX)

d) bis(1-α-naphthyl-6-methoxy-2-quinoline) trimethinecyanine perchlorate (IX), with an absorption maximum at 638 mμ;

e) bis(1-o-methoxyphenyl-5,6-benzo-2-quinoline) trimethinecyanine perchlorate (X), with an absorption maximum at 646 mμ.



(X)



Absorption curves of dyes. 1) Bis(1-p-hydroxyphenyl-6-hydroxy-2-quinoline)trimethinecyanine iodide; 2) bis(1-p-hydroxyphenyl-6-hydroxy-2-quinoline)trimethinecyanine bromide; 3) bis(1-α-naphthyl-6-methoxy-2-quinoline)trimethinecyanine iodide; 4) bis(1-α-naphthyl-6-methoxy-2-quinoline) trimethinecyanine perchlorate; 5) bis (1-o-methoxyphenyl-5,6-benzo-2-quinoline)-trimethinecyanine perchlorate.

The absorption curves of the dyes, taken in ethanol solution using an automatically recording SF-2M spectrophotometer, are shown in the figure. Judging from the absorption maxima of the indicated symmetrical carbocyanine dyes, support is given to the known tenet that the anion is practically without effect on the color, and the shift in the absorption maxima lies within the limits of error of the spectrophotometric measurements. Two hydroxy groups (in the 6-position and that found in the radical containing the N-heteroatom) gave a substantial bathochromic effect (by 24 mμ) when compared with the unsubstituted carbocyanine. Alkylation of the hydroxy groups gives a slight hypsochromic effect.

EXPERIMENTAL

1-p-Hydroxyphenyl-6-hydroxyquinaldinium perchlorate (I). A mixture of 4 g of p,p'-dihydroxydiphenylamine (m. p. 162°), 2.5 ml of hydrochloric acid (d 1.19) and 40 ml of water was charged into a three-necked flask, fitted with a dropping funnel, stirrer, and a condenser. Then 10 ml of vinyl butyl ether (b. p. 93.7°) was added dropwise in 30 minutes with stirring. After this the reaction mass was heated

at 60-70° on the water bath for 1 hour, in which connection it was observed that longer heating than this leads to increased tar formation and a reduction in the yield of quaternary salt. The dark brown reaction mixture was cooled in ice, and after 3-4 hours, the water layer was separated from the tar. To convert the salt to the iodide, the hot filtrate was treated with excess 20% potassium iodide solution, then boiled with activated carbon, and filtered. The filtrate on cooling deposited yellow needle crystals of the quaternary salt. After recrystallization from alcohol the salt melted at 258-260°. Yield 1.6 g (20%). To obtain the bromide, the salt was treated with potassium bromide solution. The bromide was obtained as greenish-yellow tablets with m. p. 290-293° (decomp.). Yield 38%.

Found %: I 33.28, 33.36; N 3.93. $C_{16}H_{14}O_2NI$. Calculated %: I 33.47; N 3.69.

Found %: Br 23.22, 23.60. $C_{16}H_{14}O_2NBr$. Calculated %: Br 23.98.

1-α-Naphthyl-6-methoxyquinaldinium iodide (II). A mixture composed of 4.72 g of p-methoxy-α-naphthylamine, 4 ml of hydrochloric acid (d 1.19), 3.2 g of paraldehyde and 5 ml of benzene was heated in a sealed tube on the boiling water bath for 6 hours. At the end of reaction the tube contents represented a brown mobile mass. The reaction product was digested with ether and then dissolved in 15 ml of alcohol. The hot alcohol solution was then treated with 20 ml of concentrated potassium iodide or potassium perchlorate solution. After boiling for a short time with activated carbon the solution was filtered, evaporated slightly, and again filtered from some tar. After 1 day the quaternary salt deposited from the solution as a yellow powder. The salt after recrystallization from water had m. p. 235-236°. The yield of the iodide was 1 g (25%). The yield of the perchlorate was 1.1 g (30%). The melting point of the perchlorate was 225-226°.

Found %: I 29.79, 29.58; OCH_3 7.48, 7.15. $C_{21}H_{18}ONI$. Calculated %: I 29.70; OCH_3 7.29.

Found %: Cl 8.81, 8.85. $C_{21}H_{18}ONCl$. Calculated %: Cl 8.88.

1-o-Methoxyphenyl-5,6-benzoquinaldinium perchlorate (IV). A mixture of 5 g of o-methoxyphenyl-β-naphthylamine, 2 g of paraldehyde, 2 ml of hydrochloric acid (d 1.19) and 15 ml of benzene was heated in a sealed ampul for 3 hours on the boiling water bath. The ampul contents, representing a brown viscous mass, were digested with ether. The solid residue remaining in the ampul was dissolved in hot alcohol. The alcohol solution was treated with 20 ml of saturated aqueous potassium perchlorate solution and 10 ml of water, in which connection a yellow-orange precipitate was obtained, which dissolved when heated. The hot solution was filtered, and the filtrate on cooling deposited the quaternary salt as a yellow-orange powder with m. p. 192°. The quaternary salt is readily soluble in alcohol, benzene, and hot water, and is practically insoluble in ether. Yield 2.55 g (33%).

Found %: Cl 8.68, 8.72. $C_{21}H_{13}O_5NCl$. Calculated %: Cl 8.87.

SUMMARY

1. The reaction of p,p'-dihydroxydiphenylamine, p-methoxyphenyl-α-naphthylamine and o-methoxyphenyl-β-naphthylamine with paraldehyde and with vinyl butyl ether gave the previously unknown quaternary salts: 1-p-hydroxyphenyl-6-hydroxyquinaldinium iodide (bromide), 1-α-naphthyl-6-methoxyquinaldinium iodide, and 1-o-methoxyphenyl-5,6-benzoquinaldinium perchlorate.

2. Symmetrical carbocyanines were synthesized from the indicated salts, and their absorption curves in the visible region of the spectrum were taken.

LITERATURE CITED

1. G. T. Pilyugin and Z. Ya. Krainer, Doklady Akad. Nauk SSSR 81, 609 (1951); Author's Certificate No. 94,015 (USSR) (1952); G. T. Pilyugin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1953), p. 1068;* Author's Certificate No. 105,287 (USSR) (1957); G. T. Pilyugin and B. M. Gutsulyak, Author's Certificate Nos. 103,319 (1956) and 109,979 (1957).

*Original Russian pagination. See C. B. translation.

2. G. T. Pilyugin, E. P. Opanasenko, and S. V. Shinkorenko, Zhur. Obshch. Khim. 27, 1015 (1957);* 28, 1316 (1958).*
3. G. T. Pilyugin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1952), p. 353.*
4. W. Konig, Ber. 55, 3293 (1924); F. M. Hamer, J. Chem. Soc. (1927), p. 2796.
5. G. T. Pilyugin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1952), p. 512.*

* Original Russian pagination. See C. B. translation.

DERIVATIVES OF PHOSPHINIC AND PHOSPHINOUS ACIDS

XII. SOME MIXED ESTERS OF ETHYLPHOSPHINIC ACID AND THEIR BIOLOGICAL ACTIVITY

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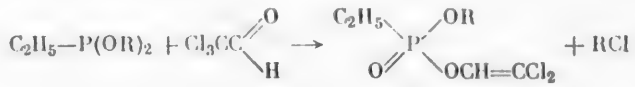
The reaction of phosphites with α-halocarbonyl compounds has been studied by various authors [1-7]. The mechanism of these reactions is still quite obscure and is treated differently by different investigators. Apparently, the polarity of the chemical bonds of the reagent, and also the character of the conjugation, both exert important influence on the direction of the reaction [8]. From the standpoint of elucidating the mechanism of the reaction it seems of interest to study the reaction of α-halocarbonyl compounds with esters of alkylphosphinous acids. These reactions should also be of interest in connection with the fact that they serve as a way of obtaining derivatives of alkylphosphinic acids with mixed functions. Earlier, it had been shown that biological activity could be expected of such compounds; up to now compounds with a high anticholinesterase activity [9-11] have been synthesized.

In this paper we report on some compounds possessing antibacterial activity. In the nature of first results we describe the reaction of the simpler esters of ethylphosphinous acid with chloral.



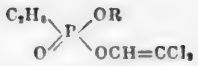
Other than the esters of ethylphosphinic acid, we failed to obtain any other products from the reaction. The obtained esters are listed in Table 1. To prove the presence of a double bond in the molecule we employed the technique of adding chlorine. This resulted in obtaining the mixed alkyl 1,2,2,2-tetrachloroethyl esters of ethylphosphinic acid (Table 2). The yield of these esters was quite small. This is explained by the fact that the starting alkyl 2,2-dichlorovinyl esters of ethylphosphinic acid taken for chlorination undergo polymerization with exceeding ease (even in the presence of hydroquinone). Noncombustible films were obtained when the indicated esters are polymerized.

The esters listed in Tables 1 and 2 possess both antibacterial and anticholinesterase activity. The antibacterial activity is manifested against gram-positive bacteria (staphylococci, streptococci, diphtheria bacteria). The chlorinated products possess a comparatively greater activity, which can be seen from the following example: compound 4 (Table 1) is active toward the above indicated bacteria at a dilution of 1:1000, with a toxicity (intravenous) of 0.91 mg/kg (on white mice), while compound 4 (Table 2), with a toxicity of 3 mg/kg, is active at a dilution of 1:10,000, i.e., by a matter of 10 times.* All of the esters are strong myotics.

* For the detailed results of investigating the antibacterial and anticholinesterase activity of all of the compounds given here see the paper by S. M. Vyaseleva, I. V. Zaikonnikova, and co-workers in "Transactions of the State University for the Improvement of Cure Treatments," Kazan, 1959.

TABLE 1

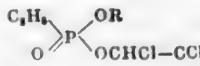
Alkyl 2,2-Dichlorovinyl Esters of Ethylphosphinic Acid



Expt. No.	R	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		%P		Yield (in %)	Solubility in water
					Calc.	Found	Calc.	Found		
1	CH_3	119—120° (13)	1.3364	1.4695	45.42	45.68	14.10	13.55, 13.65	67	1 : 70
2	C_2H_5	95—96 (0.2)	1.2787	1.4643	50.04	50.35	13.30	13.57, 13.66	83	1 : 150
3	n-C_3H_7	99.5—100.5 (0.5)	1.2284	1.4622	54.66	55.31	12.55	12.20, 12.05	80	1 : 400
4	iso-C_3H_7	87—88 (0.3)	1.2261	1.4587	54.66	55.08	12.55	12.57, 12.37	76	1 : 300
5	n-C_4H_9	108—109 (0.4)	1.2087	1.4602	59.07	59.16	11.88	11.95, 11.85	80	1 : 700
6	iso-C_4H_9	98—101 (0.3)	1.1995	1.4602	59.07	59.58	11.88	11.81, 11.73	70	1 : 900

TABLE 2

Alkyl 1,2,2,2-Tetrachloroethyl Esters of Ethylphosphinic Acid



Expt. No.	R	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		%P		Yield (in %)	Solubility in water
					Calc.	Found	Calc.	Found		
1	CH_3	101—102° (0.28)	1.4813	1.4828	55.62	55.89	10.69	10.60, 10.53	19	1:500
2	C_2H_5	103.5—104 (0.2)	1.4150	1.4768	60.24	60.68	10.20	10.46, 10.36	14	1:700
3	n-C_3H_7	115—117 (0.3)	1.3686	1.4747	64.87	65.60	9.74	9.58, 9.47	19	1:2000
4	iso-C_3H_7	99—102 (0.25)	1.3637	1.4713	64.87	65.18	9.74	9.71, 9.63	25	1:3500
5	n-C_4H_9	120—122 (0.3)	1.3273	1.4720	69.49	70.06	9.34	9.37, 9.53	18	1:4000
6	iso-C_4H_9	116.5—120 (0.35)	1.3249	1.4717	69.49	70.10	9.34	9.30, 9.17	13	1:5000

Compound 4 (Table 2) and some of the others also possess insecticidal activity, causing a 100% kill of flies after 5-minute contact at a dosage of 0.25 g of active substance per m^2 (according to the data obtained by the Central Scientific Research Institute for Disinfection).

EXPERIMENTAL

1. Preparation of mixed alkyl 2,2-dichlorovinyl esters of ethylphosphinic acid. To the dialkyl ester of ethylphosphinous acid, diluted with dry ether, was slowly added in drops, with cooling (− 2 to − 5°) and stirring, an equivalent amount of chloral, diluted with dry ether. The reaction was run in a carbon dioxide atmosphere. When all of the chloral had been added the temperature of the reaction mixture was allowed to rise at room temperature, where it was stirred for another hour. Then the solvent was removed, and the obtained ester was vacuum-distilled (in the presence of hydroquinone). The obtained esters are colorless liquids with a characteristic odor, and are soluble in alcohol and ether.

2. Preparation of mixed alkyl 1,2,2,2-tetrachloroethyl esters of ethylphosphinic acid. A mixture of the alkyl 2,2-dichlorovinyl ester of ethylphosphinic acid and a small amount of hydroquinone in carbon tetrachloride solution (2 volumes of CCl_4 per volume of taken ester) was placed in a three-necked flask, fitted with a stirrer and a thermometer. Chlorine was then passed through the solution at 14-18° until the theoretical weight increase was obtained. Then the reaction mixture was kept at room temperature for 1 hour. After removal of the solvent in vacuo (without heating) the substance was vacuum-distilled. The obtained esters are slightly yellow liquids with a characteristic odor. They are soluble in alcohol and in ether.

SUMMARY

1. The reaction of chloral with some esters of ethylphosphinous acid was studied. Some alkyl 2,2-dichlorovinyl esters of ethylphosphinic acid were obtained in this manner.

2. The addition of chlorine to the synthesized esters gave mixed alkyl 1,2,2,2-tetrachloroethyl esters of ethylphosphinic acid.

3. All of the obtained esters possess anticholinesterase and antibacterial activity to different degree and are also strong myotics.

The alkyl 2,2-dichlorovinyl esters of ethylphosphinic acid polymerize easily.

LITERATURE CITED

1. W. Perkow, Ber. 87, 755 (1954); 88, 662 (1955).
2. A. N. Pudovik and N. M. Lebedeva, Doklady Akad. Nauk SSSR 101, 889 (1955).*
3. A. N. Pudovik, Zhur. Obshch. Khim. 25, 2173 (1955).*
4. N. Kreutzkamp and H. Kayser, Chem. Ber. 89, 1614 (1956).
5. J. F. Allen and O. H. Johnson, J. Am. Chem. Soc. 77, 2871 (1955).
6. M. S. Kharasch and I. S. Bengelsdorf, J. Org. Chem. 20, 1356 (1955).
7. I. S. Bengelsdorf, J. Org. Chem. 21, 475 (1956).
8. A. I. Razumov, Zhur. Obshch. Khim. 29, 1635 (1959).*
9. A. I. Razumov, O. A. Mukhacheva, and I. V. Zaikonnikova, Zhur. Obshch. Khim. 27, 754 (1957).*
10. A. I. Razumov, E. A. Markovich, and O. A. Mukhacheva, Chemistry and Utilization of Organic Phosphorus Compounds [in Russian] (Moscow, 1957), p. 194.
11. A. I. Razumov and M. A. Aluf, Authors' Certificate No. 102,461 (USSR) (1955).

* Original Russian pagination. See C. B. translation.

REACTION OF HEXAETHYLDIPLUMBANE WITH ALKYL HALIDES

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In the course of making a systematic study of processes that go with the decomposition of tetraethyllead and hexaethyldiplumbane [1], we observed that the thermal stability of $(C_2H_5)_6Pb_2$ depends to a large degree on the conditions of its synthesis. It was established [2] that one of the reasons for this phenomenon is due to the formation of greater or lesser amounts of diethyllead in the synthesis of the hexaethyldiplumbane. In a number of cases, however, halogen compounds were found to be present in the unstable product. For this reason it seemed expedient to study the reaction of some halogen compounds with hexaethyldiplumbane. As study subjects we selected ethyl bromide, 1,2-dibromoethane, and 1,2-dibromopropane.

The reaction of compounds of type R_6Pb_2 with alkyl halides has been inadequately studied. The most detailed study has been made of the reaction of hexacyclohexyldiplumbane with the polyhalo derivatives of methane [3]. On the basis of this and some other studies, it is possible to conclude that the lead-containing products from the reaction are a mixture of compounds containing PbX_2, R_2PbX_2 and R_3PbX, where R is an organic radical, and X is halogen. In addition, in a number of cases compounds of type R_4Pb must apparently be considered as belonging to the products obtained from such reaction, since the patent literature indicates [4] that it is possible to convert hexaethyldiplumbane to tetraethyllead by heating it with an equimolar amount of an alkyl iodide.

Depending on the ratio of the reactants, it was established by us that it is possible to observe two phenomena. 1) In the case of equimolar amounts of alkyl halide and hexaethyldiplumbane a complex process takes place, consisting of a series of reactions, which lead to the formation of a large number of different products. 2) In the presence of catalytic amounts of alkyl halide a sharp reduction in the stability of the hexaethyldiplumbane is observed, with the result that it disproportionates in accordance with the equation:

$$2(C_2H_5)_6Pb_2 \longrightarrow 3(C_2H_5)_4Pb + Pb. \qquad (I)$$

The reaction of hexaethyldiplumbane with equimolar amounts of alkyl bromides was run at 40-70°, using n-heptane or its homologs as the solvent. Increasing the temperature in the indicated temperature range affects only the rate, and does not change the composition of the reaction products.

The experimental results are summarized in Table 1. From the data in Table 1 it follows that when $(C_2H_5)_6Pb_2$ is reacted with mono- and dihalo derivatives the main portion of the hexaethyldiplumbane is converted to tetraethyllead. In addition, from Table 1 it can be seen that, together with tetraethyllead, lead bromide, triethyllead bromide and dibromodiethyllead, metallic lead is obtained in all cases. As far as we know, the formation of lead in reactions of this type has not been reported before.

It was natural to assume that the metallic lead is formed either during the main reaction or as the result of secondary disproportionation of the hexaethyldiplumbane according to Eq. (I). The fact that we were able to show that hexaethyldiplumbane is extremely unstable in the presence of catalytic amounts of alkyl halides (see below) serves as important evidence in support of the second postulation.

The most probable route for the formation of the other lead-containing reaction products is the following. The primary reaction of hexaethyldiplumbane with 1,2-dihalo compounds is the formation of triethyllead bromide and olefin. Since the reaction goes with appreciable speed under conditions where the pure hexaethyldiplumbane is quite stable, it is difficult to assume that the process went because of the $(C_2H_5)_3Pb\cdot$ radicals obtained in the dissociation of the hexaethyldiplumbane. In addition, if the reaction went by a free radical mechanism, then the formation of the $\cdot CH_2CH_2Br$ radical, due to reaction of the $(C_2H_5)_3Pb\cdot$ with the dibromoethane, could be expected. Also, the formation of more or less complex mixtures as the result of subsequent reactions would be observed, in view of the diverse nature of the reactions between the radicals themselves and with the surrounding molecules. Actually, a smooth progress of the reaction is observed, with the formation of a molecule of triethyllead bromide and of olefin.

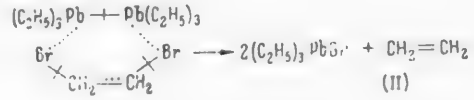
TABLE 1

Halo derivative	Reaction time (hr)	Conversion of $(C_2H_5)_4Pb$ (in %)	Reaction products*							
			$(C_2H_5)_3Pb$	$(C_2H_5)_2PbBr$	$(C_2H_5)_2PbBr_2$	$PbBr_2$	Pb	C_2H_6	C_2H_4	$n\text{-}C_4H_{10}$
Ethyl bromide	11	100	64.0	2.5	Traces	3.2	18.6	45.0, 50.8	44.0, 39.0	11.0, 10.5
1,2-Dibromoethane	2.5	100	66.0	1.1	The same	12.0	13.0	8.8, 7.0	83.0, 83.5	8.3, 9.4
1,2-Dibromopropane**	12.5	100	70.5	Traces	» »	15.4	5.1	—	—	—

* The reactions were run at 70°. The yield of lead-containing products is given in weight percent on the lead taken for reaction as hexaethyldiplumbane. The composition of the gas mixtures is given in volume percent.

** Composition of gas mixture (in volume %): propylene 90.5, ethane–ethylene fraction 9.2.

Consequently, it is most probable to assume the formation of a primary active six-membered complex, with alternately created and ruptured bonds.



(II)

In the recent studies of Ya. K. Syrkin [5] on the mechanism of chemical reactions it was shown that such transitional cyclic complexes play a very important role in many chemical reactions. In particular, for example, the reactions for the dehalogenation of 1,2-dihalo compounds can be attributed to them [6].

The triethyllead bromide, formed as the primary product, proves to be unstable under the reaction conditions; the main portion of the compound undergoes further transformations.

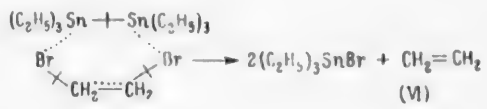
$$2(C_2H_5)_3PbBr \rightarrow (C_2H_5)_4Pb + PbBr_2 + 2C_2H_5\cdot \quad \text{(III)}$$

$$3(C_2H_5)_3PbBr \rightarrow 2(C_2H_5)_4Pb + PbBr_2 + C_2H_5Br \quad \text{(IV)}$$

$$2(C_2H_5)_3PbBr \rightarrow (C_2H_5)_2PbBr_2 + (C_2H_5)_4Pb \quad \text{(V)}$$

The reactions (III, IV, and V) are real was shown by a systematic study of the decomposition of triethyllead bromide and its analogs [7].

The scheme given above is supported by the following facts. The main reaction products when hexaethyldistannane is reacted with 1,2-dibromoethane are triethyltin bromide and ethylene; only traces of tin bromide and dibromodiethyltin are found in the reaction mixture. As a result, for the organotin analog of hexaethyldiplumbane the following reaction determines the character of the process:



$$(C_2H_5)_3Sn\text{—}Sn(C_2H_5)_3 \longrightarrow 2(C_2H_5)_3SnBr + CH_2{=}CH_2 \quad (VI)$$

The gaseous products from the reaction of hexaethyldiplumbane with 1,2-dibromopropane contain an ethane – ethylene fraction, which suggests that a part of the triethyllead bromide decomposes in accordance with Eq. (III). Along with this, the products from this reaction contain about 1 mole of gas mixture per mole of lead bromide, and consequently other routes besides reaction (III) exist for the decomposition of triethyllead bromide, not leading to the formation of gaseous substances.

An attempt to study reactions (III, IV, and V) via the decomposition of the $(C_2H_5)_3PbBr$ synthesized by us revealed that the synthesized product is a quite stable compound.

Only a partial decomposition of the product was observed when we heated the triethyllead bromide with either dibromoethane or dibromopropane in nonane medium at 70° for a long time, which stands in contradiction to the above discussed scheme. It is entirely probable that this contradiction is explained by the impossibility of creating strictly comparable decomposition conditions.

In the course of investigating the thermal stability of hexaethyldiplumbane [1] it was found that the pure substance, as well as its solutions in inert solvents, decompose in accordance with the equation:

$$(C_2H_5)_6Pb_2 \rightarrow (C_2H_5)_4Pb + 2C_2H_5 \cdot + Pb. \quad (VII)$$

Consequently, from the theoretical standpoint, a sharp change in the properties and in the scheme for the decomposition of hexaethyldiplumbane in the presence of catalytic amounts of halogen compounds, and, in particular, of dibromoethane, is a very interesting fact. Thus, for example, pure hexaethyldiplumbane,* in the absence of atmospheric oxygen, is stable for several days. At 105° it decomposes completely in 5 hours with the liberation of gaseous products. The ratio of amount of gas to metallic lead is in good agreement with Eq. (VII). The same hexaethyldiplumbane, but containing 0.1-2.0 wt. % of dibromoethane, under comparable conditions, decomposes completely in 8-10 hours at room temperature, in 2-2.5 hours at 40°, and in 20-25 minutes at 70°.

Running the decomposition of $(C_2H_5)_6Pb_2$ in evacuated ampuls, connected to a mercury manometer, revealed a practically complete absence of gas formation. The ratio between the amounts of lead and tetraethyllead was in agreement with Eq. (I).

As a result, our study reveals that in the case of hexaethyldiplumbane it is necessary to distinguish strictly the thermal decomposition reaction, proceeding in accordance with Eq. (VII), from the disproportionation reaction (I), which is caused by the action of catalysts.

It should be emphasized that only small amounts of dibromoethane (from 0.01 to 5.0 wt. %) cause a sufficiently intense disproportionation of the hexaethyldiplumbane. Further increase in the amount reduces the disproportionation rate, and in the case of equimolar amounts the mixture fails to change at room temperature even in 40-45 hours. Increasing the temperature in the latter case causes the induction period to be shortened and the appearance of concurrent reaction of the hexaethyldiplumbane with the alkyl halide, which was described in detail earlier in this paper.

Further study revealed that catalysts for the disproportionation process are apparently not only the alkyl halides themselves, but also the products of their primary reaction with hexaethyldiplumbane, namely, triethyllead bromide and dibromodiethyllead. Besides the indicated bromides, it was also established that there exists a large number of analogous compounds (metal halides, mixed organometallic compounds) that also cause disproportionation. An idea as to the relationship between the activity of these catalysts and their structure can be

*For synthesis and properties see [1].

gleaned from the data in Table 2, from which it can be seen that substances that catalyze the disproportionation of hexaethyldiplumbane are at the same time catalysts for the redistribution of radicals, studied in detail by Calingaert and co-workers [8]. Along with this, compounds that do not catalyze the redistribution of radicals (lead bromide, triethyllead hydroxide, diethyllead dihydroxide, triethyllead acetate), and also substances that do not react with hexaethyldiplumbane to form such catalysts (bromobenzene, trichlorobenzene), do not cause disproportionation. All of this permits assuming that the disproportionation of hexaethyldiplumbane under the influence of catalysts is a partial case of the reaction for the redistribution of radicals.

TABLE 2

Extent of Conversion of Hexaethyldiplumbane Under the Influence of a Catalyst

Catalyst	Amount of catalyst (in wt. %)	Reaction temp.	Reaction time (in hr)	Extent of conversion (in %)
CH_2BrCH_2Br	0.2	30°	2	7.5
	2.1	30	2	14.5
	3.8	30	2	19.7
	0.2	20	2	1.0
	0.2	40	2	16.0
	0.2	50	2	22.5
	0.3	60	0.5	19.3
C_2H_5Br	8.1	10—12	24	6.9
$(C_2H_5)_3PbBr$	3.0	10—12	24	100
$(C_2H_5)_2PbBr_2$	5.5	10—12	24	100
$(C_2H_5)_3PbCl$	3.5	10—12	24	48.0
C_2H_5HgCl	4.9	10—12	24	51.6
n-C_3H_7HgBr	4.0	10—12	24	28.0
$(C_2H_5)_3SnCl$	3.3	10—12	24	38.2
$HgCl_2$	10.0	10—12	72	35.6
$AlCl_3$	1.26	10—12	2	100

It is known that in the presence of the above-discussed catalysts, under sufficiently mild conditions, a redistribution of the radicals occurs in unsymmetrical organometallic compounds of the $R_3R'Pb$ type, leading to the formation of an equilibrium mixture of all of the possible combinations of the tetraalkyl derivatives of lead [9]. It is possible to consider hexaethyldiplumbane as being an unsymmetrical compound of specifically this type, since any of the lead atoms in this compound is linked to three ethyl radicals and one triethyllead radical, $(C_2H_5)_3Pb-R$, where $R = (C_2H_5)_3Pb$. If it is assumed that both kinds of radicals can participate with equal ease in the redistribution reaction, then the addition of one of the above discussed catalysts will cause the reaction to go, leading to the formation of an equilibrium mixture of the following compounds: $(C_2H_5)_4Pb$ (A), $(C_2H_5)_3PbR$ (B), $(C_2H_5)_2PbR_2$ (C), $C_2H_5PbR_3$ (D), and R_4Pb (E). Since the newly created compounds (B – E) also contain unsymmetrical lead atoms, the process of making the molecules more complex will continue. Along with this, the process cannot be endless, since even compounds (C, D and E) should be extremely unstable due to their containing chains composed of lead atoms. As a result, together with the process of complication, the process of decomposition of the complicated molecules will take place, for example:

$$(C_2H_5)_3Pb-\underset{\displaystyle C_2H_5}{\overset{\displaystyle C_2H_5}{\underset{|}{\overset{|}{Pb}}}}-Pb(C_2H_5)_3 \rightarrow 2(C_2H_5)_4Pb + Pb, \qquad \text{(VIII)}$$

(B) (A)

as a result of which the solitary reaction products from the redistribution of the hexaethyldiplumbane radicals are tetraethyllead and metallic lead.

And thus, by regarding the reaction for the disproportionation of hexaethyldiplumbane, going in accordance with Eq. (1), as a partial case of the reaction for the redistribution of radicals, it becomes easy to explain the extreme instability of this compound in the presence of certain substances (see Table 2).

EXPERIMENTAL

All of the experiments were run in sealed ampuls in the absence of atmospheric oxygen. The method of sealing the ampuls and of removing atmospheric oxygen from the reaction mixtures was essentially the same as that described earlier [1, 2].

Reaction of hexaethyldiplumbane with 1,2-dibromoethane. A mixture of 7.0 g (0.012 mole) of hexaethyldiplumbane and 3.1 g (0.029 mole) of the dibromoethane in 7.0 g of hexane was kept in a thermostat at 70° until the lemon-yellow color, characteristic for $(C_2H_5)_6Pb_2$, disappeared (2.5 hours). The ampul contents were cooled in liquid nitrogen, and the ampul was then connected to a gas buret and opened. The amount of gas mixture collected was 23 ml, which was analyzed by the method of gas chromatography, using silica gel as the adsorbent (see Table 1). The ampul contents were filtered, and the solid residue was washed with cold hexane. The filtrate was combined with the hexane extract, and the whole was then fractionated in vacuo. We obtained 5.1 g (66%) of tetraethyllead, b. p. 78° at 11 mm. The compound was identified as the triethyllead monochloroacetate, m. p. 142-143°. The mixed melting point with authentic monochloroacetate was not depressed.

In a separate experiment it was found (extraction of the mixture with 35% KOH, followed by analysis of the extract for bromide ion) that the liquid portion of the reaction mixture contains dissolved triethyllead bromide. An additional amount of this product was extracted from the solid reaction products using hot benzene. Total yield 1.1%. M. p. 102°. The mixed melting point with the pure substance was not depressed.

The solid reaction products (lead and lead bromide) were separated by repeated extraction of the mixture with boiling water. The results of the experiment are summarized in Table 1.

Reaction of hexaethyldiplumbane with 1,2-dibromopropane. A mixture of 1.3 g (0.002 mole) of hexaethyldiplumbane and 0.45 g (0.002 mole) of the dibromopropane was placed in an ampul (volume 128 ml), connected to a mercury manometer. Atmospheric oxygen was removed from the mixture in customary manner [1], and the ampul was evacuated and sealed. Then the ampul was kept in a thermostat at 70° for 3.5 hours, during which time the pressure increased from 3 to 98 mm of Hg. Using the procedure described in the previous experiment, the reaction mixture was worked up to give tetraethyllead (70.5% yield, based on lead), lead bromide (15.4%), and lead (5.1%). As a result, 1 mole of liberated $PbBr_2$ corresponds to about 1 mole of gas mixture.

The data on the reaction of hexaethyldiplumbane with 1,2-dibromopropane and with ethyl bromide in n-heptane medium are given in Table 1.

Reaction of hexaethyldistannane with 1,2-dibromoethane. A mixture of 6.2 g (0.015 mole) of hexaethyldistannane and 2.8 g (0.026 mole) of the dibromoethane was kept in a thermostat at 180° for 3 hours. The gaseous reaction products were analyzed by the method of gas chromatography (silica gel was used as the adsorbent). Found (in %): ethylene 90.5, ethane 9.2, butane 0.3.

The reaction mixture was fractionally distilled in vacuo. Here we collected 6.3 g (75%) of triethyltin bromide, b. p. 108-111° at 20 mm, $n^{20}D$ 1.5263. Literature data [10]: b. p. 105-107° at 15 mm, $n^{20}D$ 1.5240.

Treatment of the bromide with 20% KOH solution gave 2.6 g of triethyltin hydroxide, m. p. 43-44°. Literature data [11]: m. p. 43-44°. The residue from the distillation of the $(C_2H_5)_3SnBr$ was dissolved in alcohol and then treated with concentrated ammonia. Here we collected 0.2 g of infusible diethyltin oxide, proving to be insoluble in organic solvents, which on treatment with concentrated HCl gave diethyltin dichloride, m. p. 83° (from hexane). Literature data [12]: m. p. 84°.

Decomposition of triethyllead bromide in solvents. A solution of 2.5 g of triethyllead bromide in 10 ml of 1,2-dibromoethane was kept in a thermostat at 70° for 6.5 hours. The reaction mixture was worked up in customary manner to yield 0.3 g of lead bromide; yield 8.9% (based on lead). We also collected 30.0 ml of gas mixture, which analyzed (in mole %): ethane 20.3, ethylene 74.0, and butane 5.7.

The decomposition of 1.7 g of triethyllead bromide in 10 ml of n-nonane (8.5 hour at 70°) gave 0.28 g of lead bromide; yield 9.4% (based on lead). The composition of the gaseous reaction products was (in %): ethane 51.2, ethylene 41.8, and butane 7%.

Disproportionation of hexaethyldiplumbane. A charge of 0.1 g of 1,2-dibromoethane was placed in an ampul and then cooled in liquid nitrogen. The ampul was evacuated (0.5-1 mm Hg), after which 5.0 g (0.0085 mole) of hexaethyldiplumbane was added in drops. Then the ampul was sealed and allowed to warm up in the dark. When the dibromoethane concentration equalled 2 wt. %, the separation of metallic lead was observed as soon as the temperature reached 15-17°.

After 1 day the reaction mixture was filtered. The filtrate was practically pure tetraethyllead. The yield was 4.0 g (98.0%). B. p. 81° at 12 mm.

The metallic lead was washed repeatedly with ether, after which it was dissolved in nitric acid and determined by the molybdate method. Weight of Pb 1.1 g (97.0%).

The absence of gas formation when the disproportionation was run at 23, 40 and 70° was shown by running the reactions in evacuated ampuls, connected to a mercury manometer. An increase in the pressure was not observed during reaction.

The effect of temperature and of the dibromoethane concentration on the rate of hexaethyldiplumbane disproportionation is shown in Table 2.

SUMMARY

1. We investigated the reaction of hexaethyldiplumbane with equimolar amounts of ethyl bromide, 1,2-dibromoethane and 1,2-dibromopropane, leading to the formation of tetraethyllead, lead bromide, triethyllead bromide, dibromodiethyllead, and metallic lead. A reaction scheme was proposed.

2. The reaction of hexaethyldistannane with 1,2-dibromoethane was examined. Here the main reaction products are triethyltin bromide and ethylene.

3. It was established that besides the thermal decomposition reaction: $(C_2H_5)_6Pb_2 \rightarrow (C_2H_5)_4Pb + Pb + 2C_2H_5^{\bullet}$, hexaethyldiplumbane is also capable of undergoing disproportionation in accordance with the reaction: $2(C_2H_5)_6Pb_2 \rightarrow 3(C_2H_5)_4Pb + Pb$, caused by the action of catalysts. Catalysts for the disproportionation reaction are metal halides of the $AlCl_3$ type, mixed organometallic compounds [for example, $(C_2H_5)_3FbCl$], and also substances that react with hexaethyldiplumbane to yield the above indicated catalysts (for example, 1,2-dibromoethane).

LITERATURE CITED

1. G. A. Razuvaev, N. S. Vyazankin, and N. N. Vyshinskii, Zhur. Obshch. Khim. 29, 3662 (1959).*
2. G. A. Razuvaev, N. S. Vyazankin, and N. N. Vyshinskii, Zhur. Obshch. Khim. 30, 959 (1960).*
3. F. Hein, E. Nebe, and W. Reimann, Z. anorg. u. allgem. Chem. 251, 125 (1943).
4. U. S. Patent 2,555,891 (1951); Chem. Abs. 46, 523 (1952).
5. Ya. K. Syrkin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1959), p. 238.*
6. Ya. K. Syrkin, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1959), p. 390.*
7. G. Calingaert, H. Shapiro, F. J. Dykstra, and L. Hess, J. Am. Chem. Soc. 70, 3902 (1948).
8. G. Calingaert, H. A. Beatty, and H. Soroos, J. Am. Chem. Soc. 62, 1099 (1940).
9. G. Calingaert and H. A. Beatty, J. Am. Chem. Soc. 61, 2748 (1939).
10. H. Gilman and C. E. Arntzen, J. Org. Chem. 15, 994 (1950).
11. A. N. Nesmeyanov, K. A. Kocheshkov, and V. P. Puzyreva, Zhur. Obshch. Khim. 7, 118 (1937).
12. K. A. Kocheshkov, Zhur. Obshch. Khim. 4, 1359 (1934).

* Original Russian pagination. See C. B. translation.

DECYANOETHYLATION OF N-CYANOETHYLATED α-AMINO ACIDS AND THEIR DERIVATIVES

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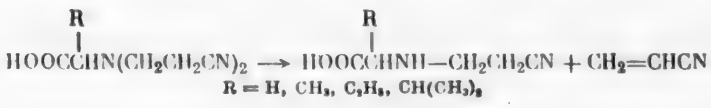
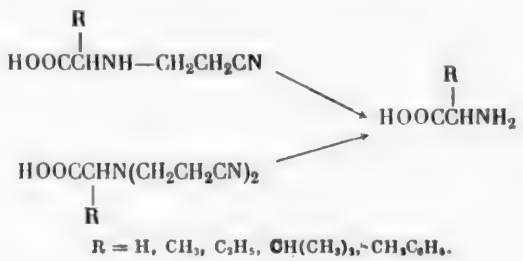
The purpose of the present work was a study of the lability of the bond between the cyanoethyl group and the nitrogen atom in N-cyanoethylated α-amino acids and their derivatives. On this subject the literature contains only the report that when N,N-dicyanoethylalanine is heated above its melting point, the substance solidifies and then melts again at the temperature corresponding to the melting point of N-monocyanoethylalanine [1] and that the hydrolysis of N,N-dicyanoethyl-α-amino acids forms N-monocarboxyethyl-α-amino acids [2].

We studied the decyanoethylation of some N-monocyanoethyl- and N,N-dicyanoethyl-α-amino acids, their esters, amides, and hydrazides, N-monocyanoethyl- and N,N-dicyanoethylglycylglycine, and N,N'-dicyanoethyl-2,5-diketopiperazine. In the investigation of decyanoethylation it was particularly important to find a method of removing a cyanoethyl group from dicyanoethyl derivatives of α-amino acids. We observed that one of the two cyanoethyl groups on the nitrogen atom may be removed readily. It was eliminated by heating dicyanoethyl-α-amino acids with aqueous solutions of tertiary amines (trimethylamine, triethylamine, pyridine, and quinoline) or an equivalent amount of caustic alkali. The reaction proceeded according to the scheme:



In some cases (derivatives of alanine and α-aminobutyric acid) this reaction occurred even with simple heating of an aqueous solution, though the yield was low. Monocyanoethyl derivatives of alanine and α-aminobutyric acid were also obtained by pyrolysis of the corresponding dicyanoethyl derivatives at 170°.

When dicyanoethylated amino acids were heated with amino acids in the presence of caustic alkali, rearrangement of the cyanoethyl groups occurred. Since cyanoethylation of amino acids is a reversible reaction, it was found that by choosing suitable conditions it was possible to eliminate the cyanoethyl groups completely from monocyanoethyl and dicyanoethyl derivatives of α-amino acids:



The yield of completely decyanoethylated products reached 80%. Agents for this reaction are ammonia, hydrazine, dimethylamine, diethylamine, and piperidine. Other amines, such as methylamine, ethylamine, and ethylenediamine, may also be used for this purpose. A 2-10% aqueous solution of ammonia gave good results in decyanoethylation. An increase in the ammonia concentration decreased the yield of decyanoethylation products. The action of gaseous and alcoholic ammonia did not give positive results. When esters, amides, and the hydrazide of cyanoethylate glycine were decyanoethylated with 10% aqueous ammonia solution, in addition to elimination of the cyanoethyl groups, there was also hydrolysis of the ester, amide, and hydrazide groups to a carboxyl.

It should also be noted that N-monocyanoethyl and N,N-dicyanoethylglycylglycine were decyanoethylated quite readily when heated with 2-5% aqueous ammonia solution. There was no hydrolysis of the peptide bond under these conditions. Thus, there is the possibility of using a cyanoethyl group for "protecting" the amine group, for example, in the synthesis of peptides.

We observed that it was impossible to remove a cyanoethyl group from N,N'-dicyanoethyl-2,5-diketopiperazine under these mild conditions.

EXPERIMENTAL

Starting materials. Cyanoethylated α-amino acids were prepared by cyanoethylation of α-amino acids with acrylonitrile [3] and β-chloropropionitrile [4]. Cyanoethylation of the ethyl ester of glycine yielded the corresponding cyanoethylation products [5] and treatment of the latter with ammonia and hydrazine hydrate gave amides [5] and the hydrazide [6] of cyanoethylated glycine. Cyanoethylated glycylglycine and diketopiperazine were synthesized from acrylonitrile and glycylglycine or diketopiperazine [7].

N,N-Dicyanoethyl-α-aminobutyric acid, which has not been described in the literature, was obtained by the general procedure [1] in 71% yield and had m. p. 48-49° (unrecrystallized product).

Found %: N 20.16. $C_{10}H_{15}O_2N_3$. Calculated %: N 20.09.

N,N-Dicyanoethylglycylglycine, which has not been described in the literature, was obtained by the action of 7.1 g (0.07 mole) of triethylamine and 10 g (0.18 mole) of acrylonitrile on a solution of 10 g (0.07 mole) of glycylglycine in 40 ml of water. The homogeneous reaction mass was allowed to stand for a week and was then evaporated to dryness in vacuum. The oil obtained crystallized on standing. The yield of N,N-dicyanoethylglycylglycine after recrystallization from alcohol was 14 g (77.7%). The m. p. was 100-103°. The substance was readily soluble in water and hot alcohol. It gave a biuret reaction, did not give a ninhydrin reaction, and did not contain amine nitrogen that could be determined by the Van Slyke method.

Found %: N 23.20, 23.34. $C_{10}H_{14}O_3N_4$. Calculated %: N 23.52.

Decyanoethylation of N,N-dicyanoethyl-α-amino acids to N-monocyanoethyl-α-amino acids. a) About 0.01 mole of dicyanoethylated α-amino acid was heated in vacuum for 1 hour at 170°. The product obtained was dissolved in water and the monocyanoethylated α-amino acid precipitated by the addition of alcohol.

b) To a solution of the dicyanoethylated α-amino acid in 50 ml of water was added an equivalent amount of potassium hydroxide and the reaction mixture heated at 100° for 10 hours. The solution was neutralized with acetic acid and concentrated and the monocyanoethylated α-amino acid precipitated by the addition of alcohol.

c) To a solution of dicyanoethylated α-amino acid in 10-100 ml of water was added 1-4 equivalents of triethylamine, pyridine, or quinoline and the reaction mixture heated under reflux at 100° for 10 hours. The solution was evaporated to dryness in vacuum and, twice, 8-10 ml of water was added to the residue and the mixture evaporated to dryness. The solid, greasy residue was dissolved in a small amount of water and the monocyanoethylated derivative of the α-amino acid precipitated by the addition of alcohol.

d) A solution of the dicyanoethylated α-amino acid in 100 ml of water containing 5 g of trimethylamine was heated in a thick-walled stoppered bottle on a boiling water bath for 10 hours. The product was isolated as in Experiment c). The experimental results are given in Table 1.

TABLE 1

Decyanoethylation of N,N-Dicyanoethyl-α-amino Acids RCH(COOH)N-$(CH_2CH_2CN)_2$ to N-Monocyanoethyl-α-amino Acids $RCH(COOH)NHCH_2CH_2CN$

R	Reagent	Decyanoethylation product: yield (in %)	Decyanoethylation product: melting point (decomp.) found	Decyanoethylation product: melting point (decomp.) from literature data
H	Potassium hydroxide	28.5	192—193°	190—191° [3]
H	Trimethylamine	28.5	192—193	
H	Triethylamine	28.5	192—193	
H	Pyridine	47.6	192—193	
H	Quinoline	47.6	192—193	
CH_3	Heating	38.8	240—245	249—250 [3]
CH_3	Potassium hydroxide	44.4	247—249	
CH_3	Trimethylamine	38.8	247—249	
CH_3	Triethylamine	38.8	247—250	
CH_3	Pyridine	50.0	247—248	
CH_3	Quinoline	50.0	247—248	
C_2H_5	Heating	47.9	233—235	233—235 [4]
C_2H_5	Potassium hydroxide	53.5	232—235	
C_2H_5	Trimethylamine	31.9	232—235	
C_2H_5	Triethylamine	44.6	232—235	
C_2H_5	Pyridine	25.5	232—235	
C_2H_5	Quinoline	31.9	232—235	
$CH(CH_3)_2$	Potassium hydroxide	60.9	250—252	252—253 [3]

Reaction of N,N-dicyanoethyl-α-amino acids with α-amino acids. A mixture of 0.016 mole of dicyanoethylated α-amino acid, 0.010 mole of α-amino acid, and 0.026 mole (1.5 g) of potassium hydroxide was dissolved in 10-15 ml of water and heated at 100° for 10 hours. After the addition of 0.026 mole (1.6 g) of glacial acetic acid, the monocyanoacetylated α-amino acid was precipitated with alcohol. The yield of N-monocyanoethylglycine was 1.7 g. It had m. p. 192-193° (decomp.). Literature data [3]: m. p. 190-191° (decomp.). The yield of N-monocyanoethylalanine was 2 g. It had m. p. 247-249° (decomp.). Literature data [3]: m. p. 249-250° (decomp.). The yield of N-monocyanoethyl-α-aminobutyric acid was 2.7 g. The m. p. was 233-235° (decomp.), which corresponds to literature data [4].

None of the monocyanoethyl-α-amino acids gave a ninhydrin reaction or contained amine nitrogen which could be determined by the Van Slyke method.

Complete decyanoethylation. 1) N-Monocyanoethyl- and N,N-dicyanoethyl-α-amino acids. A solution of 1.5-3 g of monocyanoethyl- or dicyanoethylamino acid in 100-200 ml of 10% aqueous ammonia, hydrazine, dimethylamine, diethylamine, or piperidine was heated for 10 hours in a thick-walled stoppered bottle on a boiling water bath. The solution was evaporated to dryness in vacuum, two 8-10 ml portions of water were added to the residue, and the mixture was again evaporated to dryness. The solid, greasy residue was dissolved in a small amount of water and the decyanoethylation product precipitated by the addition of alcohol. The results of the experiments are presented in Tables 2 and 3.

2) Esters and amides of N-monocyanoethyl- and N,N-dicyanoethylglycine and N-monocyanoethylglycine hydrazide. The reaction was carried out with 10% aqueous ammonia solution. The reaction conditions and method of isolating the decyanoethylation product were as in Experiment 1. The glycine yield was 70-80%.

3) N-Monocyanoethyl- and N,N-dicyanoethylglycylglycine. The reaction and treatment of the products were carried out as in Experiment 1. a) To 2 g of monocyanoethylglycylglycine was added 120 ml of 2-3% aqueous ammonia and the mixture heated at 100° for 8-10 hours. The glycylglycine yield was 1.1 g (78.6%). The substance decomposed at 210-220° (215-220° [8]). It did not give Francois or picric acid reactions; ninhydrin and biuret reactions were positive.

TABLE 2

Decyanoethylation of N-Monocyanoethyl-α-amino Acids $RCH(COOH)NHCH_2CH_2CN$ to α-Amino Acids $RCH(COOH)NH_2$

R	Reagent	Decyanoethylation product			Analysis results for decyanoethylation product (in %)		
		yield (in %)	melting point (decomp.)		amine nitrogen by Van Slyke method	elementary analysis	calculated
			found	from literature data			
H	Ammonia	80.4	230—234°	232—236° [8]	19.2	C 32.36, 32.10 H 6.89, 6.72 N 18.62, 18.66	C 31.98 H 6.71 N 18.67
H	Hydrazine	71.4	230—234		19.2	N 18.73, 18.61	
H	Piperidine	71.4	230—234		—	—	—
CH_3	Ammonia	80.0	294—296	295 [9]	15.7	N 15.53, 15.64	N 15.72
CH_3	Hydrazine	79.8	293—295		15.7	—	
CH_3	Dimethylamine	42.6	292—295		—	—	—
C_2H_5	Ammonia	50.5	286—288	285 [10]	13.5	N 13.40, 13.32	N 13.58
C_2H_5	Hydrazine	79.8	284—287		13.6	—	
C_2H_5	Diethylamine	45.5	286—290		—	—	—
C_2H_5	Piperidine	30.3	283—284		—	—	—
$CH(CH_3)_2$	Ammonia	70.6	296—298	298 [10]	11.1	N 11.94, 12.04	N 11.96
$CH_2C_6H_5$	Ammonia	81.8	270—274	271—273 [11]	8.5	N 8.35, 8.51	N 8.48

TABLE 3

Decyanoethylation of N,N-Dicyanoethyl-α-amino Acids $RCH(COOH)N(CH_2CH_2CN)_2$ to α-Amino Acids $RCH(COOH)NH_2$ (with ammonia)

R	Decyanoethylation product		
	yield (in %)	melting point (decomp.)	
		found	from literature data
H	73.7	228—234°	232—236° [8]
CH_3	69.2	294—296	295 [9]
C_2H_5	66.6	285	285 [10]
$CH(CH_3)_2$	73.3	296—298	298 [10]

Found %: C 36.30, 36.06; H 6.48, 6.22; N 21.09, 21.13; amine nitrogen by Van Slyke method 10.7. $C_4H_8O_3N_2$. Calculated %: C 36.36; H 6.10; N 21.20; amine nitrogen 10.6.

b) To 5 g of N,N-dicyanoethylglycylglycine was added 150 ml of 5% aqueous ammonia and the mixture heated at 100° for 10 hours. The glycylglycine yield was 1.7 g (62.9%). The substance decomposed at 210-220°.

SUMMARY

The decyanoethylation of N-cyanoethylated α-amino acids and their derivatives was studied.

When two cyanoethyl groups are present at a nitrogen atom, one of them is particularly labile. One cyanoethyl group is eliminated from N,N-dicyanoethyl-α-amino acids when the latter are heated with aqueous solutions of tertiary amines or caustic alkali or heated in vacuum at 170°.

When N-monocyanoethyl- and N,N-dicyanoethyl-α-amino acids are heated with aqueous solutions of ammonia, hydrazine, dimethylamine, diethylamine, and other amines, complete decyanoethylation occurs and α-amino acids are obtained.

LITERATURE CITED

1. L. McKinney, E. Uhing, E. Setzkorn, and J. Cowan, J. Am. Chem. Soc. 73, 1641 (1951).
2. L. McKinney, E. Setzkorn, and E. Uhing, J. Am. Chem. Soc. 74, 1942 (1952).
3. L. McKinney, E. Uhing, E. Setzkorn, and J. Cowan, J. Am. Chem. Soc. 72, 2599 (1950).
4. A. P. Terent'ev and P. F. Butskus, Zhur. Obshch. Khim. 27, 2591 (1957).*
5. A. P. Terent'ev and P. F. Butskus, Zhur. Obshch. Khim. 23, 1230 (1953).*
6. A. P. Terent'ev and P. F. Butskus, Zhur. Obshch. Khim. 27, 2884 (1957).*
7. A. P. Terent'ev and P. F. Butskus, Doklady Akad. Nauk SSSR 97, 851 (1954).
8. Chemists Handbook [in Russian] (1951), Vol. 2, p. 376.
9. Chemists Handbook [in Russian] (1951), Vol. 2, p. 282.
10. Chemists Handbook [in Russian] (1951), Vol. 2, p. 480.
11. Chemists Handbook [in Russian] (1951), Vol. 2, p. 790.

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DECYANOETHYLATION AND TRANSCYANOETHYLATION OF β-ALKOXY- AND β-AROXYPROPIONITRILES

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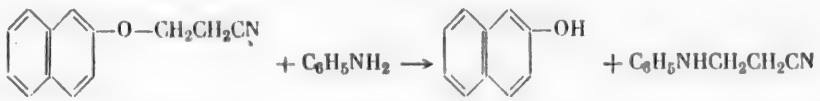
In a previous communication [1] it was shown that the reaction of aniline with β-methoxy-, β-ethoxy-, and β-phenoxypropionitriles leads to the formation of the transcyanoethylation product, namely, β-phenylaminopropionitrile. The decyanoethylation and transcyanoethylation of other β-alkoxy- and β-aroxypropionitriles were studied in the present work.

β-Phenylaminopropionitrile was obtained as a result of the reaction of aniline with monocyanoethyl derivatives of monohydric alcohols (propanol, butanol, isobutanol, sec-butanol, amyl and isoamyl alcohols, and cyclohexanol), dicyanoethyl derivatives of dihydric alcohols (ethylene glycol and 1,2-propanediol), and tricyanoethylglycerol. The reaction occurred in aqueous solution in the presence of a very small amount of sodium hydroxide or triethylamine. It was observed that in the case of the di-β-cyanoethyl ether of ethylene glycol, transcyanoethylation occurred without the addition of alkaline agents.

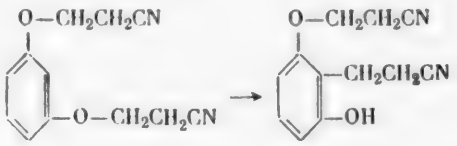
Transcyanoethylation of monocyanoethyl derivatives of o-, m-, and p-cresols and α- and β-naphthols and dicyanoethyl derivatives of dihydric phenols (pyrocatechol, resorcinol, and hydroquinone) with the aid of aromatic amines also occurred in aqueous solution in the absence of alkaline agents. As a result of the reaction it was possible to isolate both the transcyanoethylation product, β-phenylaminopropionitrile, and decyanoethylation products, namely, α- and β-naphthols and also dihydric phenols. In the case of the β-cyanoethyl ether of β-naphthol, for example, the reaction proceeded according to the scheme:



It was found that decyanoethylation occurred when β-phenoxypropionitrile, the β-cyanoethyl ethers of α- and β-naphthols, and the di-β-cyanoethyl ethers of pyrocatechol, resorcinol, and hydroquinone were heated in 5% aqueous caustic alkali solution. The decyanoethylation products were the corresponding phenols.

When the β-cyanoethyl ether of β-naphthol was heated in benzene in the presence of alkali, the cyanoethyl group was transferred from the oxygen atom to a carbon atom to form 1-(β-cyanoethyl)-2-naphthol.

Heating the di-β-cyanoethyl ether of resorcinol in methanol in the presence of sodium alcoholate led to the formation of β-hydroxy-2-cyanoethyl-3-cyanoethoxybenzene.



EXPERIMENTAL

(With the help of M. Yu. Dolmatova and A. G. Kasevich)

1. Reaction of aniline with β-alkoxypropionitriles. A mixture of 0.02 mole of β-alkoxypropionitrile, 0.1 mole (9.3 g) of aniline, and 0.025 g of sodium hydroxide in water (150 ml) was boiled under reflux for 10 hours. The reaction mixture was evaporated in vacuum on a water bath. The residue was dissolved in warm alcohol (15-20 ml) and 8-10 ml of water added. After a few days the precipitated β-phenylaminopropionitrile was collected by filtration, washed with water, and dried in air. The results of the experiments are given in Table 1.

TABLE 1

Compound decyanoethylated	β-phenylaminopropionitrile (m.p. 49-50° [2])	
	yield (in %)	melting point found
β-Propoxypropionitrile	11.9	50°
β-Butoxypropionitrile	5.5	49
β-Isobutoxypropionitrile	8.8	49
β-sec-Butoxypropionitrile	10.2	49—50
β-Amyloxypropionitrile	5.5	49
β-Isoamyloxypropionitrile	8.8	49—50
Di-β-cyanoethyl ether of ethylene glycol	14.4	49.5
Di-β-cyanoethyl ether of 1,2-propanediol	21.4	48
Tri-β-cyanoethyl ether of glycerol	22.8	49—50
β-Cyclohexyloxypropionitrile	20.2	49—50

The reaction proceeded analogously if triethylamine was used instead of sodium hydroxide.

2. Reaction of aromatic amines with β-aroxypropionitriles. A mixture of 0.01 mole of β-aroxypropionitrile and 0.1 mole of aromatic amine in water (150 ml) was boiled under reflux for 20 hours. The reaction mixture was evaporated in vacuum on a water bath. The residue was dissolved in dilute alkali and the β-phenylaminopropionitrile extracted with ether. The aqueous alkaline solution was acidified and the phenol extracted with ether. The latter was also isolated from the aqueous distillate. The results of the experiments are given in Table 2.

3. Decyanoethylation of β-aroxypropionitriles with aqueous sodium hydroxide. To 2 g of β-aroxypropionitrile was added 70 ml of 5% aqueous sodium hydroxide (or potassium hydroxide) and the reaction mixture boiled under reflux for 3 hours. The alkaline solution was acidified and the phenol extracted with ether. The results of the experiments are given in Table 3.

4. 1-(β-Cyanoethyl)-2-naphthol. A mixture of 3 g of the β-cyanoethyl ether of β-naphthol, 0.7 g of sodium hydroxide, and 10 ml of benzene was heated for 2 hours. The solid substance formed was dissolved by

TABLE 2

Starting materials		Phenols obtained by decyanoethylation				β-Phenylamino-propionitrile (m.p. 49-50° [2])	
β-cyano-ethyl ethers of phenols	aromatic amine	name	yield (in %)	melting point found*	melting point from literature data	yield (in %)	melting point found**
o-Cresol	Aniline	—	—	—	—	65.0	48—49°
m-Cresol	Aniline	—	—	—	—	68.5	48—49
p-Cresol	Aniline	—	—	—	—	68.5	48—49
α-Naphthol	Aniline	α-Naphthol	74.3	94° (subl.)	96° (subl.)[3]	70.5	48—49
β-Naphthol	Aniline	β-Naphthol	80.0	122	122—123 [3]	80.0	50
Pyrocatechol	Aniline	Pyrocatechol	—	105	104—105 [4]	72.6	49
Resorcinol	Aniline	Resorcinol	—	108—109	110.7 [4]	84.9	50
Hydroquinone	Aniline	Hydroquinone	77.0	170	170.3 [4]	74.3	48
The same	p-Toluidine	Hydroquinone	43.1	170	170.3 [4]	—	—
The same	p-Anisidine	Hydroquinone	41.3	170	170.3 [4]	—	—

* Mixed melting points of the decyanoethylation products with the corresponding naphthols and dihydric phenols were not depressed.

** Mixed melting points of the transcyanoethylation products with authentic β-phenylaminopropionitrile, obtained by the action of acrylonitrile on aniline were not depressed.

TABLE 3

Compound decyanoethylated	Decyanoethylation product			
	name	yield (in %)	melting point found	melting point from literature data
β-Phenoxypropionitrile	Phenol	64.8	38—40°	42—43° [5]
β-Cyanoethyl ether of α-naphthol	α-Naphthol	78.7	96 (subl.)	95 (subl.)[3]
β-Cyanoethyl ether of β-naphthol	β-Naphthol	87.0	120—121	122—123 [3]
Di-β-cyanoethyl ether of pyrocatechol	Pyrocatechol	77.2	103—103.5	104—105 [4]
Di-β-cyanoethyl ether of resorcinol	Resorcinol	26.7	106—109	110.7 [4]
Di-β-cyanoethyl ether of hydroquinone	Hydroquinone	50.5	170—171	170.3 [4]

the addition of 12-15 ml of water. The aqueous layer was separated from the benzene layer and acetic acid added to it to precipitate the reaction product. The latter was collected by filtration, washed with water, and recrystallized from alcohol. The yield of 1-(β-cyanoethyl)-2-naphthol was 1.5 g (50%) and the m. p. 142°, which agrees with literature data [6]. A mixed melting point with 1-(β-cyanoethyl)-2-naphthol obtained by the action of acrylonitrile on β-naphthol was not depressed.

Found %: N 7.23. $C_{13}H_{11}ON$. Calculated %: N 7.10.

5. 1-Hydroxy-2-cyanoethyl-3-cyanoethoxybenzene. A solution of 8 g of the di-β-cyanoethyl ether of resorcinol and 1.5 g of sodium in 15 ml of methanol was heated under reflux on a water bath for 24 hours. After evaporation of the methanol in vacuum, the colored oily residue was dissolved in 25 ml of 3% aqueous sodium hydroxide. The alkaline solution was extracted twice with ether, acidified with dilute hydrochloric acid, and then extracted three times with ether. The latter extract was washed several times with water and the solvent evaporated. The dark-brown residue was recrystallized twice from aqueous alcohol. The yield of 1-hydroxy-2-

cyanoethyl-3-cyanoethoxybenzene was 2.6 g and the m. p. 157-159° (m. p. 160-161° [7]). A mixed melting point with 1-hydroxy-2-cyanoethyl-3-cyanoethoxybenzene obtained by the action of acrylonitrile on resorcinol was not depressed.

SUMMARY

Transcyanoethylation occurred when β-alkoxy- and β-aroxypropionitriles were treated with aromatic amines.

Heating β-aroxypropionitriles in aqueous caustic alkali solution yielded decyanoethylation products.

When the β-cyanoethyl ether of β-naphthol and the di-β-cyanoethyl ether of resorcinol were heated in the presence of alkaline agents, a cyanoethyl group was transferred from an oxygen atom to a carbon atom.

LITERATURE CITED

1. P. F. Butskus and G. I. Denis, Nauch. Doklady Vysshei Shoky Khim., 743 (1958).
2. A. F. Bekhli, Doklady Akad. Nauk SSSR 113, 588 (1957).°
3. Chemists Handbook [in Russian] (1951), Vol. 2, p. 658.
4. Chemists Handbook [in Russian] (1951), Vol. 2, p. 426.
5. Chemists Handbook [in Russian] (1951), Vol. 2, p. 796.
6. A. Hardman, J. Am. Chem. Soc. 70, 2119 (1948).
7. G. Misra and R. Asthana, Lieb. Ann. 609, 240 (1957).

° Original Russian pagination. See C. B. translation.

AURINTRICARBOXYLIC ACID AND ITS REACTION WITH BERYLLIUM SALTS*

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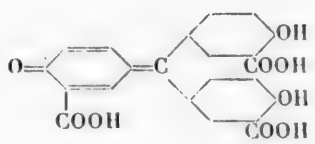
Aurintricarboxylic acid



was first proposed as an analytical reagent in 1925 [1]. It is readily synthesized [2] from accessible reagents and therefore, in the form of the ammonium salt, which is known as "Aluminon", it has found quite wide application as a reagent for aluminum [3], some rare elements [4], beryllium [5], etc. Despite this, up to now, there has been no sufficiently full investigation of the acid itself and its reaction with metals.

First it should be stated that a worthless attempt to study the reaction of aurintricarboxylic acid with Al^{3+} was made by Thrun [6], who tried to calculate the value of K and demonstrate the constancy of the ratio:

$$K = \frac{(\text{free } Al_2O_3)\cdot(\text{free aurintricarboxylic acid})}{(\text{total } Al_2O_3)\cdot(\text{lake})},$$

which should not be constant according to the Law of Mass Action. Babko [7] studied the indicator change of the reagent in the pH region around 13 and found the value pK = 13.1 by a simplified method. Starting from the position of the inflection on the optical saturation curve, he came to the conclusion that the aluminum complex has a 1 : 1 composition and found that its instability constant equals 10^{-13}, assuming that the complex arising in an acid medium is formed from anions of the dye produced at pH 13. Molot and Kul'berg [8] confirmed that the aluminum complex has a 1 : 1 composition, but they represented the reaction product differently; no data were presented on its instability constant. In the recently published work of Serdyuk, et al. [9], it was concluded that there are two beryllium – aluminon complexes with 1 : 1 (at pH 5) and 3 : 1 (at pH 7) compositions. There is no proper confirmation of this fact in the work as there are no data on the properties of the reagent itself. Thus, the problem examined requires investigation and we consider that this should begin with a study of aurintricarboxylic acid itself.

1. Changes in aurintricarboxylic acid connected with a change in the solution pH. With a change in pH, the dye studied changed color several times; therefore, optical investigation methods were very convenient in

* Work reported at the Eighth Conference on the Chemistry of Complex Compounds (Kiev, May, 1959).

this case. Preliminary experiments showed the following: a) at pH < 3 the dye precipitated practically completely; the supernatant solution had a weak yellow color; b) at pH 3.5-5, the dye acquired a pink-red color and the absorption curve had a maximum at λ = 515 mμ; c) over the range pH 6-11, the dye had only a weak bright yellow color; d) at pH 12, the dye became red-violet with λ_{max} = 545 mμ; the color had a tendency to fade with time and turn yellow; at pH 13-13.5 the initial red color also weakened slightly, but did not disappear completely; e) the dye was almost completely decolorized in strongly alkaline solution corresponding to 6-8 N NaOH.

The absorption curves for forms b, c, and d of the dye are given in Fig. 1. The change in optical density at λ = 520 mμ with changes in pH are shown in Fig. 2.

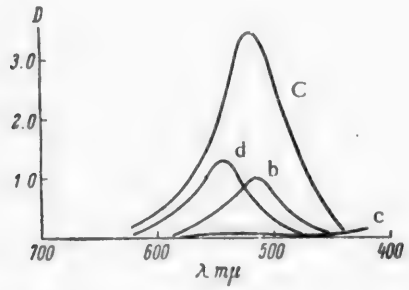


Fig. 1. Optical density curves for aurintricarboxylic acid solutions at the following pH values: b) 4.35; c) 7.0; d) 13.6; and also for the beryllium complex C at pH 4.35. (The dye concentration and layer thickness for which the values are given are $c = 1 \cdot 10^{-3}$ M and l = 0.5 cm).

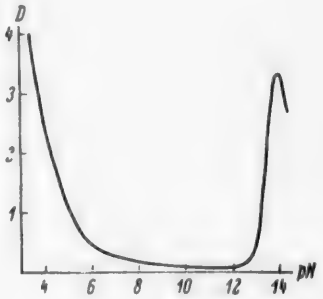
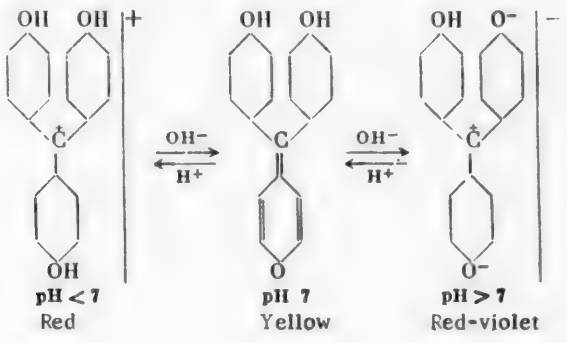
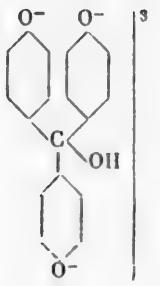


Fig. 2. Change in optical density of aurintricarboxylic acid solution at λ = 520 mμ in relation to pH. (The dye concentration and layer thickness for which the values are given are $c = 1 \cdot 10^{-3}$ M and l = 1.0 cm).

According to the theory of Dilthey [10], triarylmethane dyes become deeper in color when the quinoid grouping disappears from them and a triarylcarbonium ion appears. Thus, I. S. Ioffe [11] explained the deeper color of acid and alkaline solutions of aurin and some of its derivatives in comparison with the color of a neutral solution by these processes.

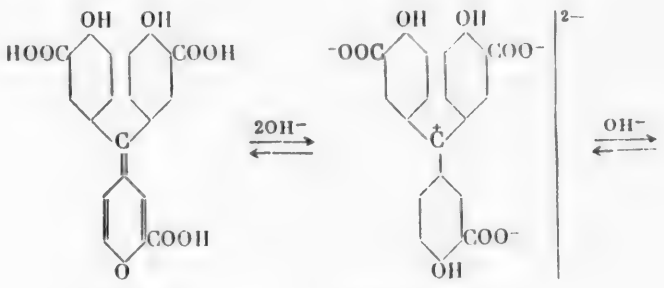


He ascribed the complete decolorization of the dye in strongly alkaline solution to the formation of a colorless carbinol derivative, which could arise only at an extremely high concentration of hydroxyl ions.



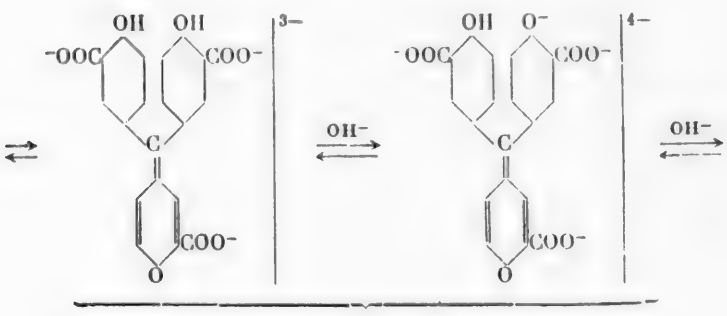
Similar opinions are held by a number of authors [8, 12, 13].

Analogous considerations may be used to explain the processes mentioned above, which occur when a solution of aurintricarboxylic acid is gradually made alkaline. The scheme which seems most probable to us is presented below.

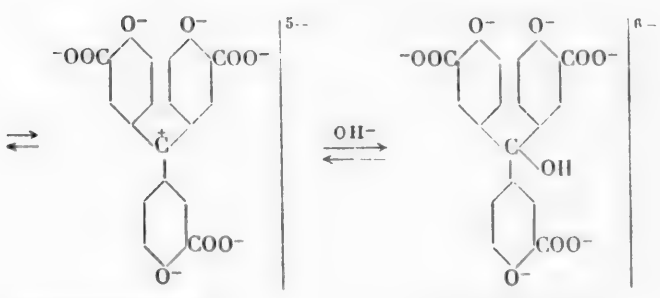


a) Precipitate
pH < 3

b) Pink-red form
pH 3.5-5



c) Yellow form
pH 6-11



d) Red-violet form
pH 12-13.5

e) Colorless form
6-8 N NaOH

In this scheme the most deeply colored substances b and d correspond to structures containing a triphenylcarbonium ion; the others have a quinoid structure or are derivatives of triphenylcarbinol. It seems to us that the change from a to b is connected with almost simultaneous dissociation of two carboxyl groups as they are in different nuclei and cannot affect each other appreciably. In any case, these successive stages of the dissociation cannot be distinguished by optical methods. Judging by the very wide range of its existence, form c apparently corresponds to two successive stages, which cannot be distinguished optically either. Forms "b", "c", and "d" are most interesting for analytical purposes. A study of these forms and also their interconversions was the purpose of the first stage of our investigation.

Aurintricarboxylic acid was first purified. It was dissolved in alkali and precipitated with hydrochloric acid and the precipitate collected by filtration, washed with water and then an alcohol-ether mixture, and dried at 25°. All the liquids used in the work were first filtered carefully. The optical density was measured on a UM-2 monochromator. The solutions were not thermostatted. The absorption temperature was 20 ± 1°.

The data used for constructing the curve in Fig. 2 were obtained as follows. A dye solution of known concentration was mixed with an equal volume of buffer mixture (simply with alkali solution for high pH values), the pH value checked with a hydrogen or glass electrode, and then the steady optical density at λ = 520 mμ measured (in some cases it was necessary to wait for up to 2 days). These data are presented in Table 1.

TABLE 1

Change in Optical Density of Aurintricarboxylic Acid Solution At λ = 520 mμ in Relation to the pH Value

Expt. No.	pH	D found	D calc.	Expt. No.	pH	D found	D calc.
1	3.40	0.90	0.87	11	12.83	0.02	0.03
2	3.95	0.57	0.62	12	13.12	0.04	0.07
3	4.51	0.40	0.36	13	13.22	0.05	0.08
4	4.96	0.27	0.24	14	13.51	0.10	0.12
5	5.69	0.12	0.17	15	13.62	0.14	0.14
6	6.74	0.07	0.10	16	13.78	0.20	0.18
7	7.12	0.07	—	17	13.92	0.28	—
8	8.30	0.06	—	18	13.97	0.33	—
9	9.56	0.05	—	19	14.40	0.27	—
10	10.72	0.03	—				

Footnote. In Experiments 1-10, l = 1 cm and $c_{dye} = 2.25 \cdot 10^{-4}$ M; in Experiments 11-19, l = 0.1 cm and $c_{dye} = 1 \cdot 10^{-3}$ M.

N. P. Komar' [14] proposed a method for calculating the molar extinction coefficients and the acid dissociation constants of dyes with indicator properties from the data of optical measurements on solutions of these dyes at different pH values. By applying the formulas he derived to the data in the first part of Table 1, we found the following mean values: ϵ_{520} (form b) = 4650 ± 400; ϵ_{520} (form c) = 650 ± 100; K_2 (transition b ⇌ c) = $(1.3 \pm 0.5) \cdot 10^{-4}$. It was not possible to apply the same formulas to the data in the second-half of the table as too sharp an increase in the optical density with comparatively small changes in pH resulted in us obtaining almost identical values which had to be subtracted one from the other and this produced such great errors in the differences that the calculation results were completely unreliable. For this reason, the values of ϵ_{520} (form d) and K_4 (transition c ⇌ d), which interested us, were determined approximately from the limiting value of the optical density in Experiment 18 and using the fact that the rising section of the curve in Fig. 2 lies within the limits of the pH values 12.83 - 13.97 and is quite symmetrical; this made it possible to consider pK_4 as equal to the pH at which the optical density reaches half of the limiting value. It was found that ϵ_{520} (d) = $\frac{0.33}{0.1 \cdot 10^{-3}}$ = 3300 and $K_4 = 2 \cdot 10^{-14}$. Together with the experimental values of the optical density, Table 1 gives values calculated by means of the constants derived; their agreement may be considered satisfactory. Babko [7] found the value $8 \cdot 10^{-14}$ for K_4, but this is much further from agreement with our experimental data.

II. Reaction of aurintricarboxylic acid with beryllium salts. A) In the acid region. Preliminary experiments showed that when a beryllium salt was added to an aurintricarboxylic acid solution, over the pH range 4-7 the optical density of the mixture increased considerably for all wavelengths and the absorption maximum was displaced from 515 to 520 mμ. This demonstrated an interaction between the components of the mixture and appeared externally as a change in the dye color from pink or yellow to bright red. Careful experiments showed that over the pH range 4-8.5, the reaction product had a constant absorption curve with a constant maximum. This indicated that a single complex exists under these conditions, contrary to the conclusions of L. Serdyuk [9] and made it possible to use appropriate methods of determining composition, which were developed for the study of one complex. The relation between the complex yield and the solution pH is illustrated in Fig. 3, which shows that the highest value of ΔD, which is linearly related to the amount of complex formed, corresponds to pH 4; however, at this pH the solutions were unstable and tended to deposit a precipitate. Therefore, it was decided to study complex formation at pH 4.35; the wavelength chosen was λ = 520 mμ, corresponding to the absorption maximum of the complex.

Tests of a whole series of buffer mixtures (citrate, acetate, Trilon, etc.) showed that to a certain extent they all reacted with beryllium, decreasing the optical density of the systems studied. Therefore, for all the solutions, the chosen pH value was established by the introduction of small amounts of acid or alkali, which was quite rapid, especially when a glass electrode was used.

TABLE 2

Values of $\Delta D = D - D_0$ Obtained at a Constant Dye Concentration of $6 \cdot 10^{-5}$ M, which Corresponds to $D_0 = 0.12$ and Varying Beryllium Concentrations (λ = 520 mμ, pH 4.35, l = 1 cm)

$c_{Be} \cdot 10^5$	ΔD		Difference
	exptl.	calc.	
0.8	0.02	0.02	0.00
1.6	0.03	0.04	+0.01
2.4	0.07	0.09	+0.02
4.0	0.10	0.10	0.00
6.0	0.13	0.12	−0.01
8.0	0.18	0.14	−0.04
24.0	0.22	0.23	+0.01
40.0	0.23	0.23	0.00
60.0	0.26	0.26	0.00
80.0	0.27		
240.0	0.28		
400.0	0.30		
600.0	0.30		

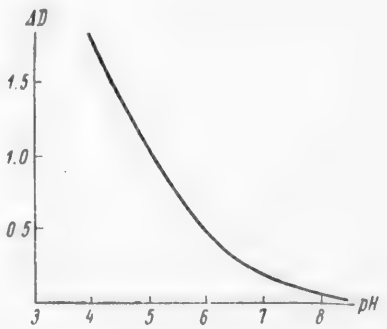


Fig. 3. Relation between complex yield (ΔD) and pH ($c_{Be} = 1 \cdot 10^{-3}$ M, $c_{dye} = 2 \cdot 10^{-3}$ M, λ = 520 mμ, and the layer thickness is adjusted to l = 0.3 cm).

The composition of the compound formed was determined by the slope method of Harvey and Manning [15], which was previously shown to be applicable to systems containing more than one colored component [16]. The results obtained are illustrated in Fig. 4, which shows that the slopes of the two lines are practically the same, establishing the ratio of the coefficients in the complex-formation reaction as 1:1. It should be noted that a second, independent method of determining the composition of the complex, based on an analytical investigation of the saturation curve [20], led to the same conclusion on the composition.

The results of a series of experiments which may be used to construct a saturation curve are given in Table 2; this table also gives the values of ΔD calculated from the approximate hyperbolic equation ($y = \Delta D$, $x = c_{Be} \cdot 10^5$), $8.6\ y^2 + 2 \cdot (8.0 + x) \cdot y - 0.6\ x = 0$, obtained from the experimental data by the method of least squares. The completely satisfactory agreement of the experimental and calculated data demonstrates the hyperbolic nature of the saturation curve, which, in its turn, indicates the absence of stepwise complex formation. The limiting optical density (D_{lim}) reached in the experiments makes it possible to determine directly the molar extinction coefficient of the complex.

$$\varepsilon_{520}(c) = \frac{D_{lim}}{l \cdot c_{dye}} = \frac{0.42}{1.6 \cdot 10^{-5}} = 7000.$$

With the composition of the complex established, it is possible to write provisionally for the complex-formation process: Dye + Be ⇌ Complex and on this basis, the following expression may be used for calculating the provisional (with an accuracy up to one factor) instability constant of the complex:

$$K_{inst} = \frac{(c_{Be} - x)(c_{dye} - x)}{x}.$$

The value of x, i.e., the equilibrium concentration of the complex, which is required for the calculations, is readily found from the experimental data in Table 3 by means of Beer's Law

$$x = \frac{\Delta D}{l(\epsilon_C - \bar{\epsilon})},$$

where $\Delta D = D - D_0$, i.e., the deviation of the optical density from the additive value, l is the layer thickness, ϵ_C is the molar extinction coefficient of the complex = 7000 and $\bar{\epsilon}$ is the molar extinction coefficient of the dye at pH 4.35, which equals $\frac{0.12}{1.6 \cdot 10^{-5}} = 2000$.

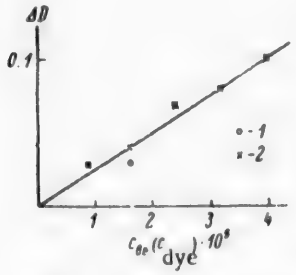


Fig. 4. Data for determining the composition of the complex by the slope method. 1) First series: c_{Be} = const = $6 \cdot 10^{-5}$ M; 2) second series: c_{dye} = const = $6 \cdot 10^{-5}$ M; λ = 520 mμ, pH 4.35, l = 1.0 cm.

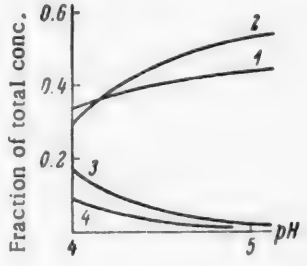


Fig. 5. Distribution of total beryllium concentration between different forms of particles in relation to pH. 1) $BeOH^+$; 2) $Be_3(OH)_3^{3+}$; 3) Be^{2+}; 4) Be_2OH^{3+}.

The instability constant calculated in this way for beryllium concentrations varying over the range $8 \cdot 10^{-6}$ to $6 \cdot 10^{-4}$ M was found to be very steady and equal to $(6.1 \pm 0.3) \cdot 10^{-5}$ (average of 9 values). It seems to us that the stability of the constant demonstrates the absence of stepwise complex formation under the experimental conditions and the accuracy of the composition established for the complex. The constant is provisional as the values of $(c_{Be} - x)$ and $(c_{dye} - x)$ in the calculations were taken for equal equilibrium concentrations of particles forming the complex, while at constant pH, in this case there is no equality, but only proportionality; this can be eliminated when the form of the particles constituting the complex has been determined.

The great similarity of the absorption curves of the dye and the complex at the pH values of 4-4.5 indicates that the doubly charged dye anion (form b) participates in complex formation. Forms c are eliminated as they are almost colorless and could hardly give a colored complex with beryllium, which has no chromophoric action. If beryllium combined with form d, which exists in an extremely alkaline medium, then the optimal yield of complex would correspond to some intermediate pH value, for example, 6-8, which is not in agreement with experimental data (see Fig. 3). Thus, form d is also eliminated.

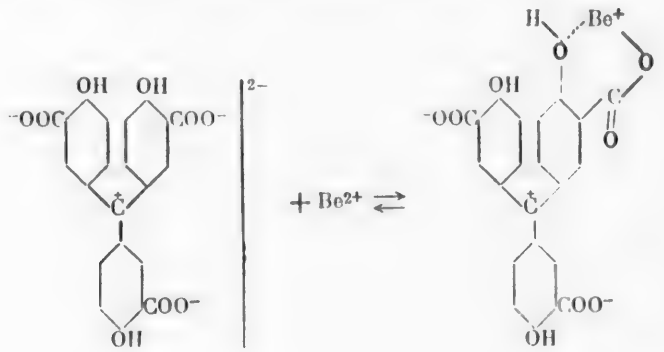
The form of the beryllium particles is a more complex problem as, according to available literature data, in acid solutions beryllium exists in at least four forms. The relation between these is given by the following expressions:

$$BeOH^+ \rightleftarrows Be^{2+} + OH^-, \quad K = 5 \cdot 10^{-11}\ [17]$$
$$Be_2OH^{3+} \rightleftarrows 2Be^{2+} + OH^-, \quad K = 3 \cdot 10^{-11}\ [18]$$
$$Be_3(OH)_3^{3+} \rightleftarrows 3Be^{2+} + 3OH^-, \quad K = 5 \cdot 10^{-32}\ [19]$$

By using this, it is possible to calculate the ratio between the concentrations of the particles for any pH value. The change in the ratio in relation to pH is shown in Fig. 5. This shows that the relative concentration of $BeOH^+$ and $Be_3(OH)_3^{3+}$ ions increases over the pH range 4-5 and therefore they cannot be considered as components of the complex as in this case the curve of the complex yield would have a maximum. In actual fact, this curve (Fig. 3) falls monotonically and, therefore, it is necessary to choose between Be^{2+} and Be_2OH^{3+} ions, whose relative concentration also falls monotonically. We finally arrive at the Be^{2+} ion as calculation for the reaction

$$Be_2OH^{3+} + 2\,Dye \rightleftharpoons complex,$$

which follows from the established component ratio of 1 : 1, gives a constant with considerable variation. Thus, the complex-formation reaction is most probably represented as follows:



This representation assumes the formation of an uncharged particle. In actual fact, the colored complex did not move at all in an instrument for studying ion transference.

TABLE 3

Weakening of Aluminum Color with the Addition of Beryllium Salt in the Alkaline Region (pH 13.6, λ = 545 mμ, c_{dye} = $= 5 \cdot 10^{-4}$ M, $D_0 = 0.39$, l = 0.3 cm)

$c_{Be} \cdot 10^4$	$\Delta D = D_0 - D$
1.0	0.00
2.5	0.05
4.0	0.09
5.0	0.12
7.4	0.15
10.0	0.22
20.0	0.32

Calculations show that at pH 4.35 the doubly charged dye anion, which is necessary for complex formation, represents 0.26 of the total concentration of free dye (considering the equilibrium between forms b and c). Considering the equilibria from [19], [17], and [18], it is possible to establish that at the same pH value the concentration of simple Be^{2+} ion is 0.09 of the total amount of beryllium. If we now multiply the values $(c_{dye} - x)$ and $(c_{Be} - x)$ by 0.26 and 0.09, respectively, they will represent the equilibrium concentrations of the particles forming the complex studied, the true instability constant of which is then found to equal $(1.4 \pm 0.1) \cdot 10^{-6}$. The activity coefficients are taken to equal unity, as is customarily done for sufficiently dilute solutions.

B. In the alkaline region. When a beryllium salt is added to an alkaline solution of aluminon, the color of the latter is weakened, but the optical density curve retains its previous form and the maximum is unchanged at λ = 545 mμ. Corresponding data are presented in Table 3. The beryllium apparently reacts with the weakly colored form c and gives an almost colorless complex, due to which the equilibrium of the dye is displaced toward a decrease in the colored form d. Therefore, the degree of decolorization may be a measure of the amount of colorless complex formed. However, mathematical treatment of the data in Table 4 showed that with the provisional limiting value $\Delta D = 0.39$,

the saturation curve could not be described satisfactorily by a hyperbola of the second order. This indicates the great complexity of the processes occurring here in comparison with the acid region; it is possible that step-wise complex formation occurs here. The complexity of the process is also shown by the extreme slowness with which equilibrium is established both in pure dye solutions and in mixtures of them with beryllium, as 48 hours is often required for this. It is possible that in this case the processes are not purely ionic. Therefore, the study of this system presents considerable difficulties. On the other hand, the reaction examined in the alkaline region can hardly be considered for analytical use as it would involve extremely accurate stabilization of the pH (Tables 1 and 2 show that the optical density increases by a factor of 6-7 over the narrow working range of pH values from 13.2 to 14.0), causing unjustifiable technical difficulties. In view of these considerations, we will limit ourselves to stating that there is undoubted interaction of a beryllium salt and aluminon at pH 13.5, without a detailed investigation of it.

SUMMARY

1. The behavior of aurintricarboxylic acid over the pH range 4-14 was studied. The acid dissociation constants were calculated and also the molar light absorption coefficients at λ = 520 mμ for the anions. It was observed that the color of freshly prepared alkaline solutions of the dye weakened with time.

2. Over the pH range of 4-6 and quite a wide range of beryllium concentrations there was only one complex with aurintricarboxylic acid with a 1:1 composition, and its structure was established.

3. Over the pH range of 13-14 there was also interaction of beryllium with the dye, but this was not studied in detail due to the low probability of its application in analysis.

4. The complex formed in an acid medium may be used both for objective photometric determinations at pH 4.3 and for visual determination at pH 6-7.

LITERATURE CITED

1. L. Hammet and C. Sottery, J. Am. Chem. Soc. 47, 142 (1925).
2. J. Scherrer and W. Smith, J. Res. Nat. Bur. Stand. 21, 113 (1938); D. Holaday, J. Am. Chem. Soc. 62, 989 (1940); W. Smith, E. Sager, and I. Siewers, Analyt. Chem. 21, 1334 (1949).
3. O. Winter, W. Thrun, and O. Bird, J. Am. Chem. Soc. 51, 2721 (1929); L. Brucker and P. Belk, Z. analyt. Chem. 88, 133 (1932); G. Cox, E. Schwartze, R. Hahm, and R. Unangst, Ind. Eng. Chem. 24, 403 (1932); P. Roller, J. Am. Chem. Soc. 55, 2437 (1933); V. Peshkova, Tr. IREA 14, 88 (1935); L. Adamovich and A. Zagorul'ko, Zavodskaya Lab. 8, 1315 (1939); L. Kul'berg and É. Robinskaya, Zavodskaya Lab. 9, 145 (1940); S. Fainberg and T. Zaglodina, Zavodskaya Lab. 14, 1109 (1945), etc.
4. R. Corey and H. Rogers, J. Am. Chem. Soc. 49, 216 (1927); J. Yoe, J. Am. Chem. Soc. 54, 1022 (1932); G. Beck, Mikrochem. Acta 2, 287 (1937), etc.
5. A. Middleton, J. Am. Chem. Soc. 48, 2125 (1926); G. Kosel and W. Neuman, Analyt. Chem. 22, 936 (1950); C. Luke and M. Campbell, Analyt. Chem. 24, 1056 (1952).
6. W. Thrun, J. Phys. Chem. 33, 977 (1929).
7. A. Babko, Zhur. Priklad. Khim. 12, 1560 (1939).
8. L. Molot and L. Kul'berg, Zhur. Anal. Khim. 11, 198 (1956).*
9. L. Serdyuk and G. Yavorskaya, Nauchn. Zap. Dnepropetr. GU 49, 149 (1954); L. Serdyuk and G. Fedorova, Ukr. Khim. Zhur. 24, 384 (1958).
10. L. Wizinger, Organic Dyes [Russian translation] (ONTI, 1936).
11. I. Ioffe, Zhur. Obshch. Khim. 17, 1904 (1947); I. Ioffe and L. Sukhina, Zhur. Obshch. Khim. 19, 1169 (1949).*
12. V. Kuznetsov, Zhur. Obshch. Khim. 20, 807, 816 (1950).*

* Original Russian pagination. See C. B. translation.

13. A. Kharkharov, Vestn. LGU 11, 4, 167 (1953).
14. N. Komar', Tr. Nauchno-Issl. Inst. Khim. KhGU 8, 57 (1951).
15. A. Harvey and D. Manning, J. Am. Chem. Soc. 72, 4488 (1950).
16. L. Adamovich, Tr. Khim. Fakult. i Nauchno Issl. Inst. Khim. KhGU 12, 107 (1954).
17. L.-B. Tab, 5 Aufl., 1120 (1923).
18. G. Mattock, J. Am. Chem. Soc. 76, 4835 (1954).
19. H. Kakihana and L. Sillen, Acta Chem. Scand. 10, 985 (1956).
20. L. Adamovich, Zhur. Neorg. Khim. 5, 4 (1960).

STRUCTURE OF THE COMPLEX COMPOUND $SnCl_4 \cdot 2CH_3COOH \cdot 2NH_2CH_2COOH$

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The action of stannic chloride on a solution of glycine in anhydrous acetic acid yielded the complex compound $SnCl_4 \cdot 2NH_2CH_2COOH \cdot 2CH_3COOH$ [1]. The same complex compound was obtained by the addition of two molecules of CH_3COOH to the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$. Cryoscopic measurements of the molecular weight of the compound $SnCl_4 \cdot 2NH_2CH_2COOH \cdot 2CH_3COOH$, carried out in CH_3COOH, showed that the molecular weight found was $^1/_3$ of that for the formula, i.e., the compound dissociates into three ions. On the basis of these data, the hypothesis was put forward that the mixed complex compound is the product of acid–base interaction of the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$ with CH_3COOH and that the latter, which has clearly expressed basic properties, adds to the outer sphere [1]. In other words, the compound $SnCl_4 \cdot 2NH_2CH_2COOH \cdot 2CH_3COOH$ was assigned the structure $[SnCl_4(NH_2CH_2COO)_2]^{--} \cdot 2CH_3COOH_2^+$.

Wishing to check this hypothesis, we decided to study the transference of ions in solutions of $SnCl_4 \cdot 2NH_2CH_2COOH \cdot 2CH_3COOH$ in acetic acid with the aid of the labeled preparations $NH_2CH_2C^*OOH$ and CH_3C^*OOH. We expected that under the action of an electric current the glycine present in the anion $[SnCl_4 \cdot (NH_2CH_2COO)_2]^{--}$ would move to the anode and CH_3COOH, to the cathode.

EXPERIMENTAL

$SnCl_4$, CH_3COOH, and NH_2CH_2COOH were purified as described previously [1]. The glycine and acetic acid labeled with the isotope C^{14} were not purified.

The experiments were carried out in an electrolyzer consisting of three spaces, separated from each other by thick glass diaphragms [2]. The experiments were as follows. We first prepared the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$ in which the glycine contained the isotope C^{14}. A solution of $SnCl_4 \cdot 2NH_2CH_2COOH$ in acetic acid was poured into the central space of the electrolyzer. The cathode and anode spaces were filled with solutions of the complex acid in acetic acid of the same concentration, but which did not contain radioactive carbon. After electrolysis, the radioactivity in samples of anolyte and catholyte was determined by the procedure in [3]. We electrolyzed a solution containing 3 mole % of the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$. A platinum cathode and a silver anode were used. The results of these experiments* are given in the table (current strength 1-10 ma, 50°).

The data presented show that under the action of an electric current, the glycine moved to the cathode, i.e., was present in the cation. Thus, from these experiments it follows that CH_3COOH displaces glycine into the outer sphere of the complex.

* The concentration of labelled glycine was increased successively in experiments 1, 2, and 3.

Experiment No.	Expt. duration (hrs)	Amt. of electricity (in coulombs)	Activity in counts/min	
			anolyte	catholyte
1	5	180	5	135
2	23	60	2	65
3	17	60	13	130

DISCUSSION OF RESULTS

In the work of one of us and É. Yarmukhamedova [1], the hypothesis was put forward that during the solution of the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$ in CH_3COOH, the latter adds in the outer sphere as an oxonium base to form a complex compound, namely, the electrolyte $[SnCl_4(NH_2CH_2COO)_2](CH_3COOH_2)_2$.

A study of the transference of ions in solutions of $SnCl_4 \cdot 2NH_2CH_2COOH$ in CH_3COOH showed that this compound has the structure $[SnCl_4(CH_3COO)_2](NH_3CH_2COOH)_2$, i.e., during the formation of the compound, the glycine is displaced by the acetic acid into the outer sphere of the complex. This displacement probably proceeds due to partial dissociation of the complex acid $SnCl_4 \cdot 2NH_2CH_2COOH$ to the components and the formation in CH_3COOH of another complex acid $SnCl_4 \cdot 2CH_3COOH$, which adds the displaced glycine in the outer sphere. Therefore, the equilibrium is displaced toward the formation of the reaction product of the complex acid $SnCl_4 \cdot 2CH_3COOH$ and glycine.

Our experiments on the electrolysis of solutions of the complex acid $SnCl_4 \cdot 2CH_3COOH$ in acetic acid to which glycine had been added (in the molecular ratio $SnCl_4 \cdot 2CH_3COOH : NH_2CH_2COOH = 1:1$) showed that the CH_3COOH labeled with the isotope C^{14} was transferred predominantly to the anode, i.e., it was present in the anion. These experiments show that glycine does not displace CH_3COOH from the inner sphere.

The compound $[SnCl_4(CH_3COO)_2](NH_3CH_2COOH)_2$ is formed not only by displacement of glycine molecules from the inner sphere by acetic acid, but also by the action of stannic chloride on a solution of glycine in CH_3COOH. The reaction apparently proceeds in the following way:

$$1)\ 2NH_2CH_2COOH + 2CH_3COOH \rightleftarrows 2NH_3CH_2COOH^+ + CH_3COO^-$$
$$2)\ 2CH_3COO^- + SnCl_4 \rightleftarrows SnCl_4(CH_3COO)_2^{--}$$
$$2NH_2CH_2COOH + 2CH_3COOH + SnCl_4 \rightleftarrows [SnCl_4(CH_3COO)_2]^{--} + 2NH_3CH_2COOH^+$$

Thus, our experiments on the transference of ions show that regardless of the method of preparation of the complex compound with the gross composition $SnCl_4 \cdot 2CH_3COOH \cdot 2NH_2CH_2COOH$, the acetate anions enter the inner sphere and the glycine adds in the outer sphere, i.e., the compound has the structure $[SnCl_4(CH_3COO)_2](NH_3CH_2COOH)_2$.

SUMMARY

1. The transference of ions in solutions of the compound $SnCl_4 \cdot 2CH_3COOH \cdot 2NH_2CH_2COOH$ in acetic acid was studied. It was established that glycine labeled with the isotope C^{14} is transferred to the cathode, i.e., is present in the cation. CH_3COOH labeled with the isotope C^{14} is transferred predominantly to the anode, i.e., is present in the anion.

2. It was shown that the complex compound studied has the following structure: $[SnCl_4(CH_3COO)_2]^{--}(NH_3CH_2COOH)_2^+$.

LITERATURE CITED

1. T. Sumarokova and É. Yarmukhamedova, Zhur. Obshch. Khim. 26, 3295 (1956).*
2. V. Klimov, M. Usanovich, and T. Sumarokova, Izvest. Akad. Nauk Kaz. SSR, Ser. Khim. 2/12, 3 (1957).
3. V. G. Vasil'ev, Zhur. Anal. Khim. 10, 368 (1955).*

* Original Russian pagination. See C. B. translation.

INVESTIGATION OF AROMATIC COMPOUNDS WITH A LONG SIDE CHAIN

IV. PREPARATION OF NITRO AND AMINO DERIVATIVES OF 4-TERT-BUTYL-, 4-ISOOCTYL-, AND 4-(α,α-DIMETHYLBENZYL)-PHENOL

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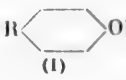
In recent years some alkylphenols have found application as intermediates in dye synthesis. It seemed interesting to use for this purpose p-tert-butyl- (Ia) and p-isooctylphenol (Ib) and 2-(p-hydroxyphenyl)-2-phenylpropane, i.e., 4-(α,α-dimethylbenzyl)-phenol (Ic), which are produced in large amounts in industry [1].

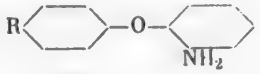


(I); (Ia) R = $(CH_3)_3C$, (Ib) R = $(CH_3)_3CCH_2C(CH_3)_2$,

(Ic) R =

The most interesting products obtained from these phenols are 2-amino-4-alkylphenols (II) and 2-amino-4'-alkyldiphenyl ethers (III).

(II)



(III)

Nitro derivatives of phenol homologs may be obtained by nitration of the corresponding phenols with dilute nitric acid in an organic solvent [2]. We nitrated tert-butyl-, isooctyl-, and dimethylbenzylphenols with 28.5% nitric acid in benzene at 10-15°. The yield of nitro compound reached 79-84%.

Nitro-substituted derivatives of diphenyl ether were obtained by reaction of potassium phenolates with o-nitrochlorobenzene at 160-170° in the presence of copper as catalyst [3]. Reducing the reaction temperature to 105° with a simultaneous increase in the reaction time from 4-5 hours to 50 hours and carrying out the process in the absence of copper, as recommended in the literature for 2-nitrodiphenyl ether [4], led only to a fall in the yield of 2-nitro-4'-butyl- and 2-nitro-4'-(α,α-dimethylbenzyl)-diphenyl ether from 80-86 to 40%. Attempts to replace metallic copper by copper sulfate did not lead to the desired results either.

Nitro compounds are readily reduced to amines by iron filings in electrolytes. However, by this method we were able to reduce only the nitro compounds obtained from p-tert-butyl- and p-isooctylphenols. The nitro derivatives of 2-(p-hydroxyphenyl)-2-phenylpropane [2-nitro-4-(α,α-dimethylbenzyl)-phenol and 2-nitro-4'-(α,α-dimethylbenzyl)-diphenyl ether] could not be reduced in any appreciable yields by iron filings alone or by zinc, tin, or stannous chloride in an acid medium. They could be reduced in high yields by hydrogen in

alcohol over Raney nickel at normal pressure and room temperature. We also reduced the derivatives of p-tert-butyl- and p-isooctylphenols and the nitro derivatives of their phenyl ethers by this method. The catalytic reduction proceeded smoothly and was normally complete in 1-2 hours. This gave high-quality amines in good yields.

EXPERIMENTAL

Nitration. Into a three-necked flask with a stirrer and thermometer were placed 0.3 mole of p-alkylphenol and 150 ml of benzene. The solution was cooled to 10-15° and over a period of 3 hours, 1 mole of nitric acid as a 28.5% solution was added dropwise with vigorous stirring. The mass was stirred at this temperature for another hour. The benzene layer was then separated from the aqueous solution, the solvent removed and the nitro compound purified either by vacuum distillation or by recrystallization from alcohol.

2-Nitro-4-tert-butylphenol formed yellow prisms with m. p. 26-26.5° and b. p. 115-116° (8 mm); the yield was 79%.

Found %: N 7.46, 7.39. $C_{10}H_{13}O_3N$. Calculated %: N 7.14.

2-Nitro-4-isooctylphenol formed a slightly yellowish liquid with b. p. 146-148° (5 mm); the yield was 83%.

Found %: N 5.54, 5.52. $C_{14}H_{21}O_3N$. Calculated %: N 5.58.

2-Nitro-4-(α,α-dimethylbenzyl)-phenol formed yellow prisms with m. p. 94.5-95.5°; the yield was 84%. According to data in [2]: b. p. 145° (15 mm).

Found %: N 5.73, 5.84. $C_{15}H_{15}O_3N$. Calculated %: N 5.45.

Preparation of o-nitrodiphenyl ethers. Into a three-necked flask with a stirrer, air condenser, and dropping funnel was placed 0.1-0.2 mole of alkylphenol. The phenol was heated to 150-160° and with vigorous stirring we added 0.05-0.15 mole of solid potassium hydroxide and 0.1-0.2 g of copper catalyst, obtained by precipitation of copper with zinc dust from copper sulfate solution. The mixture was heated until the alkali dissolved completely. Then, over a period of 1-2 hours, 0.1-0.2 mole of molten o-nitrochlorobenzene was added to the melt dropwise (possible frothing). When all the nitrochlorobenzene had been added, the mass was stirred at 160-170° for a further 5-7 hours and then poured into 400-600 ml of 4-5% sodium hydroxide solution. The nitrodiphenyl ether was extracted with benzene or ether and the extract washed with a solution of sodium hydroxide and water. The solution was dried over magnesium sulfate, the solvent removed, and the product vacuum distilled.

2-Nitro-4'-tert-butyldiphenyl ether formed slightly yellowish prisms with m. p. 46.5-47.5° and b. p. 197.5-199° (3 mm); the yield was 78%.

Found %: N 5.27, 5.44. $C_{16}H_{17}O_3N$. Calculated %: N 5.16.

2-Nitro-4'-isooctyldiphenyl ether was a viscous yellow liquid with b. p. 230-233° (17 mm); the yield was 62.5%.

Found %: N 4.29, 4.41. $C_{20}H_{25}O_3N$. Calculated %: N 4.28.

2-Nitro-4'-(α,α-dimethylbenzyl)-diphenyl ether formed yellowish prisms with m. p. 76-77°; the yield was 86%.

Found %: N 4.35, 4.15. $C_{21}H_{19}O_3N$. Calculated %: N 4.20.

Reduction of nitro compounds with iron filings in an electrolyte (method A). Over a period of 1 hour, 0.04 mole of 2-nitro-4'-tert-butyl- or 2-nitro-4'-isooctyldiphenyl ether was added in small portions to a boiling mixture of 20 g of iron powder, 3 ml of acetic acid, 25 ml of water, and 40 ml of xylene in a three-necked flask with a stirrer, thermometer, and reflux condenser. After being boiled for 5-6 hours, the mass was filtered hot and the residue washed with hot xylene. Distillation of the solvent from the filtrate yielded the amine. The product was obtained in a crystalline state in the reduction of the nitro-tert-butyldiphenyl ether, while reduction of the nitroisooctyldiphenyl ether yielded a yellow oil, which crystallized only on prolonged standing.

Amine	Reduction method	Yield (in %)	External appearance	Melting point	% N		Melting point of benzoyl derivative
					found	calculated	
2-Amino-4-tert-butylphenol	B	76	Colorless leaflets, darkening in air	153-154°	9.12, 9.30	8.48	184-184.5°
2-Amino-4-isooctylphenol	B	80	The same	129-130 [5]			
2-Amino-4-(α,α-dimethylbenzyl)-phenol	B	85	The same	131.5-131.8	6.15, 6.28	6.16	137-138°
2-Amino-4'-tert-butyldiphenyl ether	A	74.8	Colorless prisms	83-84°	5.90, 5.89	5.81	105-106°
The same	B	87.7	Reduced with hydrogen on palladium black				
The same	B	90	Reduced with hydrogen on Raney nickel				
2-Amino-4'-isooctyldiphenyl ether	A	88	Slightly yellowish liquid	B. p. 207 to 208° [2]	4.74, 4.79	4.71	
2-Amino-4'-(α,α-dimethylbenzyl)-diphenyl ether	B	90	Colorless prisms	70.2-70.8	4.85, 4.77	4.65	101-102°
2-Aminodiphenyl ether	B	95		42-43 [6]			

Reduction of nitro compounds with hydrogen on Raney nickel (method B). Into a pear-shaped 500-ml flask fixed to a shaker were placed 50-100 ml of alcohol, 0.01-0.02 mole of nitro compound, and Raney nickel (30-35% of the weight of nitro compound). When the system had been flushed with hydrogen, the shaker was switched on and hydrogen was passed into the reaction flask until absorption ceased completely. Toward the end of the reduction, the mass was heated to 40° with an electric lamp. For liberation of the amine, the reaction mass was filtered to remove the catalyst and the filtrate diluted with water. The solid amines thus precipitated were collected by filtration, washed with a small amount of alcohol, and dried with air, while the liquid 2-amino-4'-isooctyldiphenyl ether was separated in a separating funnel and then vacuum distilled.

The results of reduction of nitro compounds by the two methods are given in the table.

SUMMARY

1. By the reaction of potassium phenolates with o-nitrochlorobenzene it was possible to synthesize nitro-substituted derivatives of diphenyl ether with tert-butyl, isooctyl, and dimethylbenzyl groups in the position para to the ether group.

2. Nitration of p-tert-butyl-, p-isooctyl-, and p-(α,α-dimethylbenzyl)-phenols yielded the corresponding o-nitrophenols.

3. It was shown that it is possible to reduce homologs of 2-nitrodiphenyl ether and o-nitrophenol to the corresponding amines with hydrogen on Raney nickel at normal pressure and room temperature.

LITERATURE CITED

1. N. N. Vorozhtsov, Fundamentals of the Synthesis of Intermediates and Dyes [in Russian] (GKhI, 1955), p. 698; B. D. Kruzhalov and P. G. Sergeev, Khim. Nauka i Prom. 1, 287 (1956).
2. U. S. Patent 2,429,178; Chem. Abs. 48, 618 (1954); U. S. Patent 2,802,883, Chem. Zentr. (1958), 10206; R. C. Huston and G. W. Hedrich, J. Am. Chem. Soc. 59, 2001 (1937).
3. Synth. Org. Prep. [in Russian] (1949), Coll. 2, p. 370.
4. BIOS , 1153, 103.
5. H. E. Albert, J. Am. Chem. Soc. 76, 4985 (1954).
6. F. Ullmann, Ber. 29, 1876 (1896).

CONVERSION OF ACETOACETAMIDE TO 4-AMINO-2,4-DIMETHYL-Δ^2-TETRAHYDRO-6-PYRIDONE-3-CARBONAMIDE

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Derivatives of pyridine and hydrogenated pyridine, in particular, pyridones, carboxylic acids, and amides (for example, nicotinic acid derivatives) are acquiring ever increasing value as pharmaceutical preparations and physiologically active substances with analgesic, spasmolytic, local anesthetic, bactericidal, insecticidal, soporific, and other properties. In addition, these compounds form a group of substances which are interesting for the variety of reactions and methods of synthesis [1].

Claisen and Meyer [2] and also probably Duisberg [3] observed the condensation of two molecules of acetoacetamide with the formation of lutidonecarbonamide when the original amide was heated above its melting point. Acetoacetamide was previously a difficultly accessible substance, but is now readily obtainable from diketene [4] and so its use for the synthesis of pyridones deserves attention, especially as the products obtained would be structurally similar to nicotinic acid and may also have physiological activity.

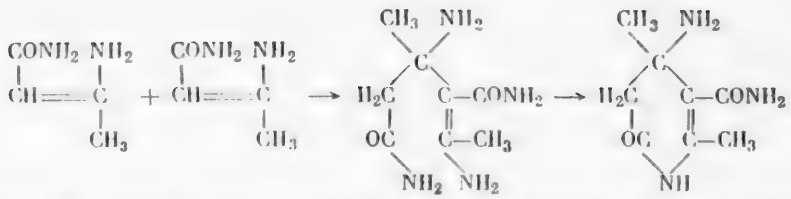
By investigation of aqueous ammonia solutions of acetoacetamide, prepared from diketene, that had been stored for a definite time, it was established that in aqueous solution at room temperature there is spontaneous condensation of the aminocrotonamide formed to 4-amino-2,4-dimethyl-Δ^2-tetrahydro-6-pyridone-3-carbonamide, which corresponded in melting point and properties to the carbonamide obtained by Chick and Wilsmore from aminocrotonamide at 118° in a stream of hydrogen [5].

The starting solution contained only acetoacetamide, ammonia, and a small amount of ammonium acetate (from acetic anhydride, which was an impurity in the diketene). After a certain time, aminocrotonamide appeared in the solution. The crystalline carbonamide isolated was a derivative with a nitrogen heteroatom since, of the three nitrogen atoms determined by the Kjeldahl method, one of them required very drastic conditions for conversion to ammonium sulfate. On the other hand, one of the nitrogen atoms was readily eliminated as ammonia during hydrolysis with alkali (but could not be determined with Nessler's reagent). The amides present in the solution are capable of forming a heterocyclic compound and the reaction of two acetoacetamide molecules or the reaction of acetoacetamide with aminocrotonamide would yield lutidonecarbonamide, i.e., a compound containing two nitrogen atoms. Only the reaction of two molecules of aminocrotonamide yields a pyridine derivative with three nitrogen atoms, namely, aminodimethyltetrahydropyridonecarbonamide. The structure was also confirmed by calculation of the molecular weight from the amount of ammonia liberated during hydrolysis or after mineralization of the substance.

The formation of the pyridonecarbonamide from acetoacetamide proceeds by several stages. In the presence of free ammonia, acetoacetamide in aqueous solution is gradually converted to aminocrotonamide.

$$CH_3COCH_2CONH_2 \xrightarrow{NH_3} CH_3C(NH_2)=CHCONH_2$$

Two molecules of the latter condense and then the heterocyclic ring is closed.



The decrease in the amount of acetoacetamide in the solution became appreciable after 5-7 days and this should be considered in using such solutions for synthesis of pyrazolones by the acetoacetamide method. However, after 3 months, the solution still contained about 50% of unchanged acetoacetamide.

EXPERIMENTAL

Preparation of acetoacetamide. With vigorous stirring, 43 g of 97.5% diketene was added dropwise to 127 ml of a cooled 18% solution of ammonia. The solution obtained contained 31.4% of acetoacetamide and 7.7% of ammonia. From the yield of 1-(2'-chloro-5'-sulfophenyl)-3-methylpyrazolone-5 from the reaction of chlorosulfophenylhydrazine with an acetoacetamide solution [4] that had been kept in the laboratory for about 3 months, it was established that the decrease in the amount of amide in solution was 50%.

Preparation of 6-amino-2,4-dimethyl-Δ^2-tetrahydro-6-pyridone-3-carbonamide. A sample (80 ml) of a solution that had been kept for 3 months and corresponded to 0.25 mole of acetoacetamide was heated gently in a water-pump vacuum until boiling ceased. The sirupy mass formed crystallized after 2 days. The crystals were readily separated from the mother liquor with acetone, in which they were difficultly soluble. Recrystallization of the mixture from an alcohol – ether mixture gave a white crystalline substance with m. p. 196° (corr.). The yield was 5 g.

The substance obtained was readily soluble in water and acetic acid, soluble in methanol and ethanol (more in the former; solubility in hot ethanol, 1.5%), and almost insoluble in boiling acetone, benzene, ether, chloroform, and molten camphor. Reactions with ferric chloride solution and Nessler's reagent were negative. An aqueous solution of the substance was neutral. Distillation with zinc dust yielded an oily liquid, which crystallized on cooling. The product was not nitrated by nitric acid, but was readily converted into a nitro derivative by the action of a mixture of nitric and sulfuric acids. A solution of the nitro compound was colorless in an acid medium and yellow in alkali.

The substance isolated from the acetoacetamide solution lost ammonia when treated with alkali. The ammonia was distilled by boiling 0.0159 g of the substance with 5 ml of sodium hydroxide (1 : 2) in 50 ml of water for 1.5 hours with the distillate caught in a trap with 50 ml of 0.01 N hydrochloric acid; the excess acid was titrated with 0.01 N alkali solution in the presence of Methyl red. The amount of ammonia determined corresponded to 1 atom of nitrogen in the compound $C_7H_{11}ON_2CONH_2$.

Found %: N 7.62. $C_8H_{13}O_2N_3$. Calculated %: N 7.65.

In a normal determination of nitrogen by the Kjeldahl method with selenium as a catalyst, a pale yellow solution was formed after 5-10 minutes. However, it was not possible to achieve complete mineralization of the compound in this way. The results varied. The analysis showed a nitrogen content of 15.95 and 17.50%, which corresponds approximately to 2 nitrogen atoms per molecule. By carrying out the analysis under drastic conditions [6], it was possible to destroy the compound completely. For this purpose, a sample (0.0238 g) was boiled for 3 hours with a mixture of 1 ml of sulfuric acid and 4 g of potassium bisulfate until the mixture was completely decolorized. The subsequent stages of the analysis were carried out by the usual methods. As a result of complete mineralization of the substance, the amount of nitrogen determined corresponded almost exactly to 3 atoms in the compound $C_8H_{13}O_2N_3$.

Found %: N 22.82. $C_8H_{13}O_2N_3$. Calculated %: N 22.95.

When the pure substance or a mixture of it with lime was heated strongly, a readily crystallizable substance with m. p. 70° sublimed. The same product was obtained by heating the substance that had first been

treated with concentrated hydrochloric acid or alkali. It is probable that this product was the starting material that had lost the carboxyl group (in analogy with other pyridine derivatives, which readily lose a carboxyl group under similar conditions).

The amine group in position 4 could not be determined by the normal methods due to its low activity [7] and steric hindrance.

Considering that only half of the acetoacetamide had reacted, the yield of aminodimethyltetrahydropyridonecarbonamide was 43.7%.

SUMMARY

In aqueous solution in the presence of ammonia, acetoacetamide is gradually converted into 4-amino-2,4-dimethyl-Δ^2-tetrahydro-6-pyridone-3-carbonamide. This conversion gave not less than 43% yield without heating or the use of hydrogen.

LITERATURE CITED

1. Heterocyclic Compounds [Russian translation] (IL, 1953), Vol. 1, Chap. 8.
2. L. Claisen and K. Meyer, Ber. 35, 583 (1902).
3. C. Duisberg, Lieb. Ann. 213, 174 (1882).
4. P. A. Levin, Zhur. Obshch. Khim. 26, 2274 (1956).*
5. F. Chick and N. Wilsmore, J. Chem. Soc. 97, 1978 (1910).
6. V. I. Esafov, Zavodskaya Lab. 21, 1160 (1955).
7. A. Holleman, Course in Organic Chemistry [Russian translation] (1939), p. 489.

* Original Russian pagination. See C. B. translation.

PHOSPHORUS-CONTAINING POLYESTER AND POLYAMIDE RESINS

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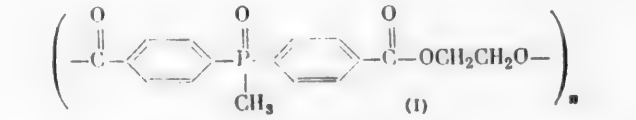
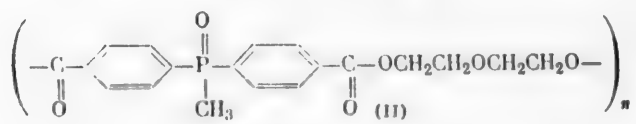
In contrast to phosphorus-containing insecticides and other physiologically active substances, up to now organophosphorus polymers have not found wide application and have not received thorough attention in the literature. However, on the basis of available data, we may conclude that some organophosphorus polymers with specific properties may be of practical interest [1-5].

The purpose of the present work was the synthesis of organophosphorus condensation polymers of the polyester and polyamide types. Ethylene glycol, diethylene glycol, hexamethylenediamine, and the ester of the dibasic carboxylic acid bis-(p-carbomethoxyphenyl)-methylphosphine oxide were used for condensation. Polymers (I), (II), and (III) are described in the work.



(I)



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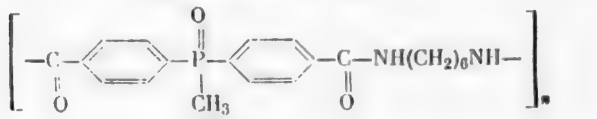

(III)

The distinctive characteristic of these polymers is the fact that units in their chains are formed by pentavalent phosphorus atoms, connected by phosphorus–carbon bonds. Thus, polymers (I) and (III) differ from Terylene and Nylon in that the terephthalic acid residue in the chain of the former and the adipic acid in the latter have been replaced by bis-(p-carboxyphenyl)-methylphosphine oxide residues.

Phosphine oxides are most resistant to heat and various chemical reagents among organophosphorus substances and in this respect they differ sharply from phosphates and phosphonates. The inclusion of a phosphorus oxide group in the chain did not decrease its stability and considering the capacity of phosphorus to reduce the chemical activity of substances, it might be expected that the polymers obtained will have a high chemical stability and physicomechanical strength.

Bis-(p-carbomethoxyphenyl)-methylphosphine oxide has been described in the literature. However, the method of preparing it is complex and, in individual stages, the intermediates in its synthesis are formed in low yields [6-8].

In the present investigation, the method of preparing the ester in separate stages was substantially changed and refined. Thus, bis-(p-tolyl)-methylphosphine oxide was obtained by the reaction of the diacid chloride of methylphosphinic acid with p-tolylmagnesium bromide.

$$CH_3POCl_2 + 2CH_3C_6H_4MgBr \rightarrow CH_3PO(C_6H_4CH_3)_2 + 2MgBrCl$$

The yield of the phosphine oxide reached 82% (with 5% excess p-tolylmagnesium bromide used).

In contrast to other investigators, we oxidized bis-(p-tolyl)-methylphosphine oxide with a hot alkaline solution of permanganate; the process was complete in 2 hours and the acid yield reached 81%.

Mixing an aqueous alcohol solution of the acid with an aqueous solution of ferric chloride yielded the iron salt, which has not been described in the literature previously.

Heating bis-(p-carboxyphenyl)-methylphosphine oxide with thionyl chloride yielded the diacid chloride (decomp. p. 64-65°). We synthesized bis-(p-carbomethoxyphenyl)-methylphosphine oxide in 73.5% yield by esterification of the acid with methanol in the presence of hydrogen chloride.

Bis-(p-carboethoxyphenyl)-methylphosphine oxide, which has not been described previously in the literature, was obtained in the same way as the methyl ester. Transesterification of the methyl ester with n-butyl alcohol gave a good yield of bis-(p-carbobutoxyphenyl)-methylphosphine oxide, which has not been described previously.

The ethylene glycol and diethylene glycol polyesters of bis-(p-carboxyphenyl)-methylphosphine oxide (I and II) were obtained by prolonged heating of the methyl ester of bis-(p-carboxyphenyl)-methylphosphine oxide with ethylene glycol and diethylene glycol in the presence of a catalyst, namely, zinc borate and pentaerythritol (first at atmospheric pressure and then in vacuum). Clear, slightly colored polyesters could be obtained only when the reaction was carried out in the absence of oxygen. Both polyesters dissolved in chloroform to form viscous solutions from which they were precipitated by the addition of absolute ether; the polyesters formed filaments when drawn from solutions.

The polyamide (III) was obtained by heating in vacuum the salt prepared by mixing hexamethylenediamine with bis-(p-carboxyphenyl)-methylphosphine oxide. The polyamide formed a brown vitreous mass, which was insoluble in ether, benzene, and chloroform; it also formed filaments when drawn from a melt. The specific viscosity of a 1% solution in m-cresol and the softening point were measured for polyesters (I) and (II) and polyamide (III).

EXPERIMENTAL

Bis-(p-tolyl)-methylphosphine oxide. With the reaction mixture stirred and cooled in ice and salt, to the Grignard reagent from 25.5 g of magnesium and 179.5 g of p-bromotoluene in 750 ml of absolute ether was added 66.5 g of the diacid chloride of methylphosphinic acid in 300 ml of ether at such a rate that the temperature did not rise above 15°. The solution was boiled for 1 hour, 300 ml of chloroform added,* and the solution again heated on a water bath for 4 hours. The reaction mass was cooled and then 400 ml of a 20% aqueous solution of ammonium chloride slowly added. The ether–chloroform layer was separated, the aqueous layer extracted twice with chloroform (100 ml portions), and the combined extracts dried with baked sodium sulfate. Evaporation of the solvent gave 99 g (82% yield) of the phosphine oxide, which melted at 105-108°, and then after recrystallization from anhydrous benzene or alcohol, it melted at 143-145°.

Bis-(p-carboxyphenyl)-methylphosphine oxide. To a solution of 130 g of permanganate in 4 liters of water was added 50 g of bis-(p-tolyl)-methylphosphine oxide and the mixture heated on a boiling water bath for 3 hours. The manganese dioxide was then removed by filtration and the solution acidified with dilute hydrochloric acid and evaporated to dryness on a water bath. The residue was washed with hot anhydrous alcohol. After removal of the alcohol, the acid, which was isolated as a viscous mass, crystallized when absolute ether was added. We obtained 51 g of acid (81.5% yield).

* For economy in solvents, before addition of the chloroform, the ether may be distilled from the reaction mixture on a water bath and then used in the reaction without purification.

After recrystallization from an alcohol – ether mixture, the bis-(p-carboxyphenyl)-methylphosphine oxide had m. p. 295°. A mixed melting point with the acid obtained by oxidation of bis-(p-tolyl)-methylphosphine oxide with permanganate in the presence of pyridine [6] was not depressed. When an aqueous solution of ferric chloride was mixed with an aqueous alcohol solution of the acid the iron salt formed a yellowish-red precipitate. The salt was insoluble in water and organic solvents and did not melt when heated to 300°.

Found %: P 9.51. $C_{45}H_{33}O_{15}P_3Fe_2$. Calculated %: P 9.13.

Bis-(p-carbomethoxyphenyl)-methylphosphine oxide. Hydrogen chloride was passed for 2 hours into a boiling solution of 33 g of bis-(p-carboxyphenyl)-methylphosphine oxide in 500 ml of anhydrous methanol and then the solution heated for a further 2 hours. Cooling the solution precipitated bis-(p-carbomethoxyphenyl)-methylphosphine oxide, which, after recrystallization from methanol, had m. p. 225° and was found to be identical with the ester obtained previously by a somewhat different method [6]. We obtained 26.5 g of ester (73.5% yield).

Bis-(p-carboethoxyphenyl)-methylphosphine oxide. Bis-(p-carboxyphenyl)-methylphosphine oxide (5 g) in 60 ml of anhydrous alcohol was esterified as described above with the difference that after treatment with hydrogen chloride, the mixture was heated for 6 hours. The alcohol was then removed by distillation and the residual thick oil dissolved in alcohol and neutralized with sodium carbonate. When absolute ether was added, the oil crystallized. After three recrystallizations from aqueous alcohol, the ester had m. p. 147-148° and was soluble in alcohol and benzene, but insoluble in water.

Found %: P 8.16. $C_{19}H_{21}O_5P$. Calculated %: P 8.62.

Bis-(p-carbobutoxyphenyl)-methylphosphine oxide. A mixture of 1.5 g of bis-(p-carbomethoxyphenyl)-methylphosphine oxide, 20 ml of butanol, and a few crystals of zinc acetate was heated at 150-160° for 6 hours. Removal of the alcohol left 1.4 g of the butyl ester with m. p. 117-120°; after recrystallization from hot aqueous methanol, the product had m. p. 122°. The butyl ester was readily soluble in ether, benzene, and alcohols, but insoluble in water.

Found %: P 7.4. $C_{23}H_{29}O_5P$. Calculated %: P 7.44.

Good results were also obtained by transesterification in the presence of sulfuric acid. When 2 g of the methyl ester, 20 g of butanol, and 8 drops of sulfuric acid were heated for 8 hours, we obtained 2 g of bis-(p-carbobutoxyphenyl)-methylphosphine oxide.

Diacid chloride of bis-(p-carboxyphenyl)-methylphosphine oxide. To 4 g of bis-(p-carboxyphenyl)-methylphosphine oxide was added 20 ml of thionyl chloride and the mixture heated on a water bath for 3 hours. The excess thionyl chloride was removed by distillation to leave the diacid chloride of bis-(p-carboxyphenyl)-methylphosphine oxide as a thick oil, which crystallized when treated with ligroin. The diacid chloride decomposed at 64-65° and was soluble in hot chloroform and carbon tetrachloride, but less soluble in ether and benzene. We obtained 2.1 g of diacid chloride.

Found %: Cl 20.75. $C_{15}H_{11}O_3PCl_2$. Calculated %: Cl 20.8.

Polyester from ethylene glycol and bis-(p-carbomethoxyphenyl)-methylphosphine oxide. To 4 g of finely ground bis-(p-carbomethoxyphenyl)-methylphosphine oxide were added 7.5 g of ethylene glycol and a few crystals of zinc borate and pentaerythritol; the mixture was stirred carefully and heated at normal pressure for 16 hours at 200-210° and 1 hour at 250°. The transesterification was complete under these conditions and the methanol and excess ethylene glycol were removed. The reaction mass was a colorless mobile liquid in the hot state. The pressure was then reduced to 10-12 mm in the apparatus and the reaction mass kept in a nitrogen atmosphere at 210° for 3 hours and for 7 hours at 260° and 1-0.5 mm. We obtained a yellowish, vitreous resin, which was soluble in chloroform, but insoluble in ether and benzene. The specific viscosity of a 1% solution in m-cresol was 0.34 at 20°. The softening point of the resin was 167-168°. The polyester was precipitated from chloroform with ether as a white crystalline substance.

Polyester from diethylene glycol and bis-(p-carbomethoxyphenyl)-methylphosphine oxide. To 1 g of bis-(p-carbomethoxyphenyl)-methylphosphine oxide were added 1.4 g of diethylene glycol and a few crystals of zinc borate and the mixture was heated at atmospheric pressure and 200-210° for 20 hours, the reaction mass cooled to 200°, the pressure in the apparatus reduced to 12 mm, and the reaction mass heated in a nitrogen

atmosphere for 3 hours at this temperature and for 20 hours at 285° and 0.5-1 mm. We obtained a vitreous mass, which was soluble in chloroform, but insoluble in ether and benzene; the specific viscosity of a 1% solution in m-cresol equaled 0.41 at 20° and the polymer softened at 97-98° and could be drawn from a melt as filaments.

Polyamide from hexamethylenediamine and bis-(p-carboxyphenyl)-methylphosphine oxide. For the condensation we required the ammonium salt of bis-(p-carboxyphenyl)-methylphosphine oxide with hexamethylenediamine and this was obtained by mixing hot alcohol solutions of hexamethylenediamine (3.04 g of hexamethylenediamine in 40 ml of anhydrous alcohol) and the acid (1 g of acid in 20 ml of alcohol). A thick oil first precipitated and crystallized on standing. The salt was collected, washed with alcohol, and dried; it had m. p. 245° (beginning of decomp.) and was soluble in water, but insoluble in alcohol.

Found %: N 7.07; P 7.16. $C_{21}H_{29}O_5N_2P$. Calculated %: N 6.64; P 7.36.

The polycondensation was carried out under the following conditions: 1 g of ammonium salt and 1 g of phenol were heated in vacuum (10 mm) for 3 hours at 270°. We obtained a brown vitreous mass which was insoluble in chloroform, ether, and benzene. The specific viscosity of a 1% solution of the polyamide in m-cresol at 20° was 0.34; the softening point was 174-175°. It could be drawn from a melt as filaments.

SUMMARY

1. We obtained two polyesters by polycondensation of bis-(p-carbomethoxyphenyl)-methylphosphine oxide with ethylene glycol and diethylene glycol and also a polyamide by condensation of bis-(p-carboxyphenyl)-methylphosphine oxide with hexamethylenediamine.

2. A method was developed for preparing bis-(p-tolyl)-methylphosphine oxide; the oxidation of this to bis-(p-carboxyphenyl)-methylphosphine oxide was refined, and several derivatives of this acid that have not been described in the literature previously were synthesized.

LITERATURE CITED

1. E. L. Gefter, Usp. Khim. 25, 162 (1956).
2. V. V. Korshak, I. A. Gribova, and M. A. Andreeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 631 (1957).*
3. V. V. Korshak, I. A. Gribova, and M. A. Andreeva, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 880 (1958).*
4. U. S. Patent 2,646,420; Chem. Abs. 47, 10276g (1953).
5. T. M. Frunze, V. V. Korshak, et al., Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 783 (1958).*
6. P. W. Morgan and B. C. Herr, J. Am. Chem. Soc. 74, 4526 (1952).
7. A. Michaelis, Lieb. Ann. 315, 97 (1901).
8. D. C. Morrison, J. Am. Chem. Soc. 72, 4820 (1950).

* Original Russian pagination. See C. B. translation.

AMINOSILANES

II. METHODS OF SYNTHESIZING SOME TETRAALKOXYSILANES

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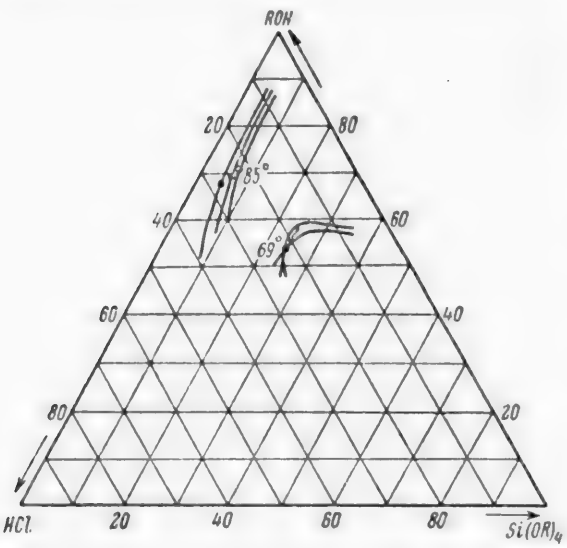
Tetraalkoxysilanes are usually obtained by the action of alcohols on halosilanes. Variants of this reaction are described in detail in the literature [1-7].

The last stage of the reaction

$$SiCl_4 + ROH \rightarrow SiORCl_3 \xrightarrow{+ROH} Si(OR)_2Cl_2 \xrightarrow{+ROH} Si(OR)_3Cl \xrightarrow{+ROH} Si(OR)_4$$

proceeds slowly and a certain excess of alcohol is required to displace the equilibrium to the right. With excess alcohol, the yield of partial esterification products is reduced practically to zero, but there is a considerable increase in the yield of fractions boiling below $SiORCl_3$. In the synthesis of tetramethoxysilane, during the distillation the hydrogen chloride evaporates and then a fraction begins to distill with a boiling point close to 69° [4] and in the synthesis of tetraethoxysilane, the analogous fraction boils at about 85° [5]. As Peppard, Brown, and Johnson [4] reported, the ternary mixture $Si(OCH_3)_4 - CH_3OH - HCl$ boils at 69°. The components of this mixture are capable of reacting together in two stages:



Change in the composition of low-boiling fractions during the fractionation of tetraalkoxysilanes.

1) Reaction of HCl with the alcohol to form methyl chloride and water; 2) hydrolysis of the ester by the water liberated, right to the precipitation of $nSiO_2 \cdot mH_2O$.

By analyzing the reaction products with a boiling point below that of $SiORCl_3$, we found that they contain considerable amounts of tetraalkoxysilanes and alcohol. By using these products we were able to increase the yields of tetraalkoxysilanes considerably. We represented the change in composition of the low-boiling fractions with temperature in the form of a ternary diagram with the coordinates $Si(OR)_4 - CH_3OH - HCl$ (figure). The analytical and graphical data for several syntheses were extremely close, which then allowed us to use the diagram constructed for rapid calculation of the mixture composition from one determined component (HCl).

In comparing the positions of the curves for the change in fraction composition with temperature for tetraethoxy- and tetramethoxysilanes, we should note that the losses of tetraethoxysilane in the low-boiling fractions are considerably lower than with tetramethoxysilane.

Having calculated the amount of free alcohol in the by-product from the diagram, with cooling and vigorous stirring, we added the equivalent amount of $SiCl_4$. By breaking up the ternary mixture, the rapid reaction made it possible to obtain further considerable amounts of the main product (10-15% of tetraethoxysilane and 25-30% of tetramethoxysilane) due to the tetraalkoxysilane present in the ternary mixture and as a result of esterification of the alcohol in the mixture.

We also developed a new method of synthesizing tetraalkoxysilanes, based on the alcoholysis of aminosilanes. The properties of silicon compounds containing an Si – N bond have not been studied adequately up to the present time [2]. In particular, there has been little study and no widespread practical application of the alcoholysis of aminosilanes. This is apparently explained by the fact that from the preparative point of view it seems more advantageous to proceed directly from compounds containing the reactive Si – Cl bond to compounds with the Si – O bond. Nonetheless, a study of the alcoholysis of some aminosilanes showed that the reactions proceed extremely smoothly and give high yields of products with a comparatively short synthesis [8-10].

The proposed method of preparing tetraalkoxysilanes was based on the exchange of chlorosilanes with amines with subsequent treatment of the aminosilanes formed with alcohols according to the scheme:

$$SiCl_4 + 8RNH_2 \rightarrow Si(NHR)_4 + 4RNH_2 \cdot HCl;$$
$$Si(NHR)_4 + 4R'OH \rightarrow Si(OR')_4 + 4RNH_2,$$

where R = CH_3, C_6H_5, $CH_3C_6H_4$, and other aliphatic and aromatic radicals.

The reactions may be carried out both by the action of alcohols on aminosilanes isolated in a pure form and without isolation of the latter, which are intermediate products.

We used this method to synthesize tetramethoxy- and tetraethoxysilanes, using derivatives of methylamine, aniline, and p-toluidine as the intermediate products. The silicon in the tetraalkoxysilanes synthesized was determined gravimetrically as SiO_2 [11], the carbon and hydrogen were determined by combustion by Pregl's method [12], the chlorine was determined by titration of the hydrolysis products with alkali, and the alkoxyl groups were determined by Zeisel's method [11].

EXPERIMENTAL

Tetramethoxysilane. a) Into a three-necked, 500-ml flask with a dropping funnel, a stirrer with a seal, and a reflux condenser [13] was placed 141 g of cooled, anhydrous methanol. Over a period of 2 hours, 170 g of silicon tetrachloride was added dropwise with the mixture stirred in the cold for the first hour and then with gradual heating to 65° on a water bath. When the vigorous evolution of hydrogen chloride had ceased, the product was distilled on a glycerol bath with the successive removal and analysis of fractions boiling over 1° ranges. The distillation yielded a product with b. p. 121-123° (68 g, 44%), a distillation residue (polymer) with b. p. above 130° (24 g), and fractions boiling below 75° (65 g). The mean SiO_2 content of the latter was 10.4% (from the data of five syntheses). These fractions were redistilled and separate distillates boiling over 1-2° ranges were analyzed. The analysis results are given in the figure, which shows that the composition of the fractions changed over comparatively narrow ranges. Analogous data for tetraethoxysilane are given in the same diagram. Treatment of the tetramethoxysilane fractions boiling below 75° with silicon tetrachloride gave an additional 46 g of tetramethoxysilane, i.e., about 30% of the initially calculated yield of the ether.

b) Into a 1000-ml, flat-bottomed flask were placed 300 ml of anhydrous benzene and 42.5 g of silicon tetrachloride. Gaseous methylamine was passed through the solution until the mixture no longer gave a reaction for unreacted $SiCl_4$ with iodide – iodate reagent (brown color with paper moistened with KI + KIO_3) [14]. The methylamine hydrochloride precipitate was removed by filtration and washed with benzene. The solution obtained (or the mixture if the precipitate was not removed) was then treated with 36 g of anhydrous methanol with stirring and slight cooling. The benzene was removed and a fraction collected with b. p. 121-123°, d^{20}_4 1.024, $n^{20}D$ 1.3690. The yield was 29.6 g (78%).

Found %: C 31.89; H 7.95; Si 17.90. $C_4H_{12}O_4Si$. Calculated %: C 31.57; H 7.89; Si 18.04.

c) Into a 1000-ml, round-bottomed flask were placed 136 g of silicon tetrachloride and 558 g of dry, freshly distilled aniline (in small portions over a period of 10-15 minutes). The flask was closed with a reflux condenser and heated on a water bath for 20-30 minutes. The reaction mixture was then distilled and a fraction collected with b. p. 121-123°, d^{20}_4 1.026, $n^{20}D$ 1.3693. The yield was 103.4 g (85%).

Found %: C 32.10; H 8.02; Si 18.29. $C_4H_{12}O_4Si$. Calculated %: C 31.57; H 7.89; Si 18.04.

Tetraethoxysilane. Into a 200-ml round-bottomed flask were placed 19.8 g of recrystallized tetraphenylaminosilane and 10.1 g of anhydrous alcohol. The reaction proceeded with considerable heat evolution. When the mixture had been stirred for a short time (5-10 minutes), the flask was placed on a water bath and the mixture heated under reflux for 15-20 minutes. The product obtained was distilled and a fraction collected with b. p. 165-167°, d^{20}_4 0.935, $n^{20}D$ 1.3857. The yield was 94.6 g (91%).

Found %: C 47.25; H 9.75; Si 13.73. $C_8H_{20}O_4Si$. Calculated %: C 46.15; H 9.62; Si 13.92.

SUMMARY

1. Processes occurring during the synthesis of tetraalkoxysilanes were investigated.

2. It was established that by additional treatment of the etherification by-products with silicon tetrachloride it is possible to achieve a considerable increase in the yield of some esters of orthosilicic acid.

3. A new method was developed for synthesizing tetraalkoxysilanes, which was based on treatment of chlorosilanes with various amines and subsequent treatment of the aminosilanes formed with alcohols.

LITERATURE CITED

1. B. N. Dolgov, Chemistry of Organosilicon Compounds [in Russian] (GKhTI, 1933).
2. K. A. Andrianov, Organosilicon Compounds [in Russian] (GKhI, 1955).
3. A. P. Kreshkov, Organosilicon Compounds in Technology [in Russian] (Promstroiizdat, 1956), 2nd edition.
4. D. F. Peppard, W. G. Brown, and W. C. Johnson, J. Am. Chem. Soc. 68, 70, 73, 76, 77 (1946).
5. L. V. Myshlyaeva, Dissertation [in Russian] (D. I. Mendeleev Moscow Chemicotechnological Institute, 1948).
6. A. P. Kreshkov and G. D. Nessonova, Zhur. Obshch. Khim. 19, 660 (1949).*
7. M. G. Voronkov and B. N. Dolgov, Zhur. Priklad. Khim. 24, 93 (1951).*
8. A. P. Kreshkov, L. V. Myshlyaeva, and L. M. Khananashvili, Author's Certificate 108,137 (1957).
9. L. M. Khananashvili, Dissertation [in Russian] (D. I. Mendeleev Moscow Chemicotechnological Institute, 1957).
10. A. P. Kreshkov, L. V. Myshlyaeva, and L. M. Khananashvili, Zhur. Obshch. Khim. 28, 2105 (1958).*
11. A. P. Kreshkov, V. A. Bork, L. V. Myshlyaeva, and G. D. Nessonova, Analysis of Organosilicon Compounds [in Russian] (GKhI, 1954).
12. K. Weygand, Experimental Methods in Organic Chemistry [Russian translation] (IL, 1951), Vol. 3, p. 46.
13. A. W. Dearing and E. E. Reid, J. Am. Chem. Soc. 50, 3058 (1928).
14. L. V. Myshlyaeva, Tr. MKhTI im. D. I. Mendeleeva 25, 29 (1957).

* Original Russian pagination. See C. B. translation.

REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

IX. EFFECT OF POSITION OF HALOGEN AND ELECTRON-DONOR SUBSTITUENT AND OF THE NATURE OF THE ELECTRON-DONOR SUBSTITUENT

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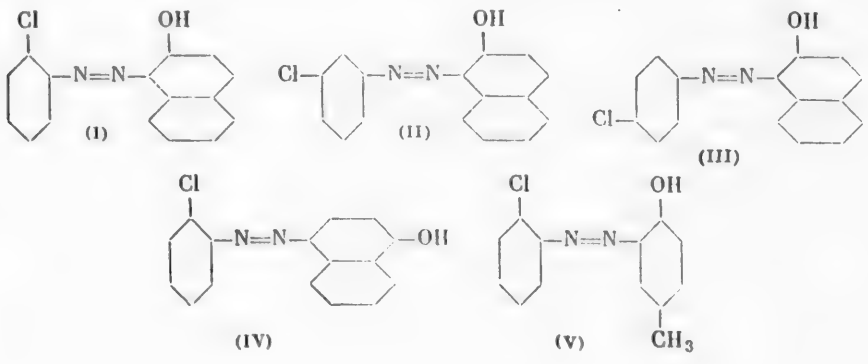
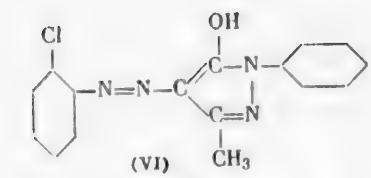
To determine the limits of applicability of the replacement of a halogen atom in azo compounds in the presence of copper salts by various substituents, we studied the reaction of sodium n-butylate with chlorine-containing hydroxyazo compounds, differing in the position of the chlorine atom and the hydroxyl group relative to the azo group and also in the nature of the hydroxyl group. In addition, experiments were carried out with chlorine-containing azo compounds in which there was a different electron-donor substituent instead of the hydroxyl group.

The effect of the position of the halogen atom and the hydroxyl group relative to the azo group was studied in experiments with 2-, 3-, and 4-chlorobenzeneazo-2'-naphthols [azo dyes (I), (II), and (III) from 2-, 3-, and 4-chloroanilines, respectively, and 2-naphthol] and with 2-chlorobenzeneazo-4'-naphthol [azo dye (IV) from 2-chloroaniline and 1-naphthol]. For a study of the effect of the nature of the hydroxyl group, data for dye (I) were compared with those for 2-chloro-5'-methyl-2'-hydroxyazobenzene, 2-chlorobenzene-(1-azo-4')-1'-phenyl-3'-methylpyrazolone-5', and 2-chlorobenzeneazoacetoacetanilide [azo dyes (V), (VI), and (VII) from 2-chloroaniline and p-cresol, 1-phenyl-3-methylpyrazolone-5, and acetoacetanilide, respectively]. As azo compounds with electron-donor substituents different from hydroxyl in the position ortho to the azo group we used 2-chlorobenzeneazo-2'-naphthylamine, 2-chlorobenzeneazo-2'-methoxynaphthalene, and 2-chlorobenzeneazo-2'-butoxynaphthalene [azo dyes (VIII), (IX), and (X) from 2-chloroaniline and 2-naphthylamine, 2-methoxynaphthalene, and 2-butoxynaphthalene, respectively].





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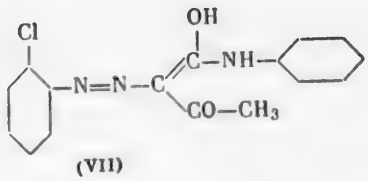

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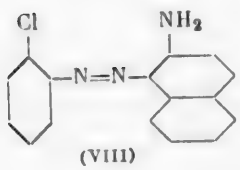

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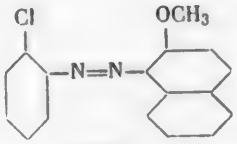

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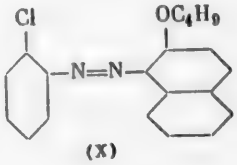


(X)

The azo dyes were treated with sodium n-butylate at 100°. The reaction was begun by adding a solution of the dye in toluene [in the case of dye (VI), in a mixture of chlorobenzene and benzene or in pyridine and in the case of dye (VII), in chlorobenzene] to a solution of sodium n-butylate and copper acetate in butanol and was ended by the addition of 10% sulfuric acid solution. The reaction mass was then diluted with benzene, washed carefully with water, and the wash waters titrated potentiometrically with silver nitrate solution for determination of the chlorine ion content (see Table 2 in Experimental), corresponding to the degree of replacement of chlorine in the original dye. The degree of replacement found in this way was checked by investigation of the reaction products.

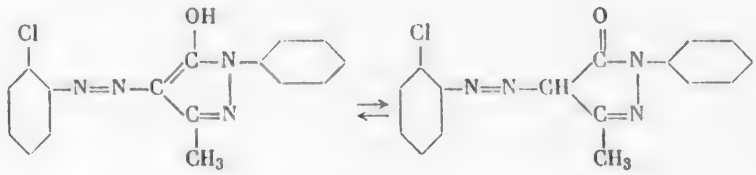
The results obtained indicate that the first condition for replacement of a halogen atom in the azo compounds is the proximity of both the halogen atom and the electron-donor substituent to the azo group. A chlorine atom in a position ortho to the azo group was not replaced when treated with the alcoholate for 8 hours at 100° in cases where the hydroxyl group was in a position para to it [dye (IV)], while chlorine atoms in the meta and para positions were not replaced even when the hydroxyl group was in the ortho position [dyes (II) and (III)].

Then, it is apparently important for a successful reaction that the electron-donor substituent in the position ortho to the azo group should contain a labile hydrogen atom. When this was absent, as in the case of methoxyl and butoxyl groups [dyes (IX) and (X)], replacement of the halogen occurred to an insignificant extent (5-7%) during prolonged treatment of up to 22 hours at 100°. Thus, there are grounds for assuming that even within the given limits, replacement occurs in a dye which has not an alkoxyl group, but a free hydroxyl group, formed during the reaction as a result of a side process, namely, dealkylation. This was confirmed to some extent by the fact that the chlorine-free product from the reaction of 2-chlorobenzeneazo-2'-methoxynaphthalene [dye (IX)] with sodium butylate, of which 6% was isolated from the reaction mass (i.e., in an amount corresponding to the degree of replacement, determined by the chlorine eliminated), was found to be 2-butoxybenzeneazo-2'-naphthol, i.e., a compound with a free hydroxyl group. It is known [1] that complex formation by alkoxyazo dyes with copper is frequently accompanied by dealkylation. The probability of this process under the conditions of our experiments is also indicated by our observation that under these conditions, i.e., when 2-chlorobenzeneazo-2'-methoxynaphthalene was treated with sodium n-butylate in the presence of copper acetate for 8 hours at 100°, the methyl residue in the ether group was replaced by butyl to form 2-chlorobenzeneazo-2'-butoxynaphthalene [dye (X)]; we cannot exclude the possibility that during this transalkylation of the alkoxyl group, it was partially dealkylated.

The third factor which is of importance in the replacement of halogen in azo compounds is apparently the capacity of the electron-donor substituent with the labile hydrogen atom to exchange the latter for metal. In the case of a hydroxyl group of a phenolic nature present in a benzene [dye (V)] and a naphthalene [dye (I)] nucleus, practically complete replacement of the halogen atom by the alkoxyl group was found after 2 hours' treatment with alcoholate at 100°. In the case of a hydroxyl group of an enol nature [dye (VII)], there was 66% reaction after 8 hours at the same temperature. In the case of an amino group [dye (VIII)], there was only 21% reaction after 8 hours. As far as we know, the replacement of chlorine in azo dyes with such azo constituents as the arilide of a β-keto acid and an amine was achieved for the first time.

As already reported [2, 3], we established that replacement of chlorine in azo compounds with a phenolic hydroxyl group as the electron-donor substituent by an alkoxyl group occurs during the reaction of copper complexes of these compounds with alcoholates in the absence of a free copper salt. It was interesting to test in this respect the copper complexes of dyes with an enolic hydroxyl group and with an amino group as the electron-donor substituents. Unfortunately, we were unable to obtain the complex of dye (VII) in a crystalline state. As regards the copper complex of dye (VIII), the reaction with it in the absence of a copper salt gave exactly the same results as experiments with the free dye in the presence of a copper salt; there was also 21% replacement of chlorine after 8 hours at 100°.

A somewhat unexpected result was obtained with dye (VI) with methylphenylpyrazolone as the azo component; when a solution of the dye in a mixture of chlorobenzene and benzene (2.5 : 1 by volume) was treated with alcoholate in the presence of copper acetate for 8 hours at 100°, no reaction occurred (chlorine ions were not detected in the reaction medium and the dye was recovered quantitatively). Assuming that under the reaction conditions the tautomeric equilibrium



is displaced completely toward the keto form, we carried out experiments with pyridine as the solvent in view of its enolizing action. However, the result obtained was the same. Since dye (VI) readily gives a copper complex and an enolic hydroxyl group evidently participates in the formation of this, we carried out the reaction with it (under the same conditions, but in the absence of free copper salt). However, no replacement of chlorine was detected in this case either. This example apparently deserves further study, which we propose to make in the near future.

EXPERIMENTAL

Starting dyes (I) - (IV), (VI), and (VIII) have been described in the literature (Table 1). Dyes (V) and (VII) were obtained by diazotization of 2-chloroaniline and coupling with p-cresol and acetoacetanilide, respectively.

TABLE 1

Starting Dyes

No.	Diazo component	Azo component	Melting point	
			found	literature data
(II)	3-Chloroaniline	2-Naphthol	161-162° (from a mixture of benzene + methanol 2 : 1)	158° [4] 155-157° [5]
(III)	4-Chloroaniline	The same	163-164.5° (from benzene)	160° [4] 162.5° [4]
(I)	2-Chloroaniline	The same	167° (from a mixture of alcohol + chlorobenzene 3 : 1)	167° [4]
(IV)	The same	1-Naphthol	183-183.5° (from alcohol)	184-185.5° [6]
(VI)	The same	1-Phenyl-3-methyl-pyrazolone-5	189.5-190° (from a mixture of benzene + methanol 1 : 1)	188° [7]
(VIII)	The same	2-Naphthylamine	155-156° (from benzene)	151° [8]

2-Chloro-5'-methyl-2'-hydroxyazobenzene [dye (V)] formed dark yellow needles with m. p. 111-112.5° after recrystallization from a mixture of benzene and alcohol (1 : 3).

Found %: C 63.34, 63.29; H 4.52, 4.57; Cl 14.39, 14.40. $C_{13}H_{11}ON_2Cl$. Calculated %: C 63.29; H 4.49; Cl 14.37.

2-Chlorobenzeneazoacetoacetanilide [dye (VII)] formed light yellow needles with m. p. 159-159.2° after recrystallization from a mixture of benzene and methanol (1 : 2).

Found %: C 60.86, 61.02; H 4.33, 4.49; N 13.28, 13.56. $C_{16}H_{14}O_2N_3Cl$. Calculated %: C 60.86; H 4.46; N 13.30.

2-Chlorobenzeneazo-2'-methoxynaphthalene [dye (IX)] was obtained by the method of Charrier and Ferreri [9]. 2-Chlorobenzeneazo-2'-naphthol [dye (I)] (1.41 g) was carefully ground with 100 ml of 30% sodium hydroxide solution and the suspension obtained heated to 60° in a flask with a reflux condenser and stirrer. At 60-65°, 31.5 g of dimethyl sulfate was added and the temperature raised to 80-85°. After 1 hour the reaction mass was diluted with 200 ml of water and the precipitate collected, washed with dilute ammonia solution and then water, and dried. The weight was 1.3 g (87%). After recrystallization from methanol, the product formed dark red prisms with m. p. 123-124°.

Found %: C 68.55, 68.53; H 4.49, 4.49; N 9.02, 9.13; Cl 11.90, 11.92. $C_{17}H_{13}ON_2Cl$. Calculated %: C 68.80; H 4.41; N 9.44; Cl 11.95.

2-Chlorobenzeneazo-2'-butoxynaphthalene [dye (X)] was obtained by transalkylation of dye (IX) (see below).

The copper complex of 2-chlorobenzeneazo-2'-naphthylamine [dye (VIII)] was obtained by Crippa's method [10]. Dye (VIII) (2.5 g) was dissolved in 250 ml of boiling alcohol and to the cooled solution was added an ammonia solution of copper sulfate, prepared by dissolving 7.5 g of copper sulfate in 12.5 ml of ammonia solution and 12.5 ml of water. A red-brown precipitate formed immediately. The mixture was heated on a water bath for 7 hours and then cooled and the precipitate collected and washed with alcohol. Black-green lustrous platelets were obtained. The weight was 2.4 g (86%) and the m. p. 128-133° (decomp.), which corresponds to the data in [11] for 2-(o-chlorophenyl)-naphtho-1',2' :4,5-triazole, formed by heating the copper complex of 2-chlorobenzeneazo-2'-naphthylamine.

Copper complex of 2-chlorobenzene-(1-azo-4')-1'-phenyl-3'-methylpyrazolone-5 [dye (VI)]. The amounts of reagent were as in the previous case, but 100 ml of dioxane was used instead of alcohol. The mixture was heated for 2 hours on a water bath and the precipitate which formed when the mixture was cooled was collected and washed with dilute ammonia, water, and hot methanol. We obtained 2.5 g (90%) of violet platelets with m. p. 254-256°; according to data in [12], m. p. 263° (decomp.).

Reaction of azo dyes with sodium butylate. An experiment with dye (I) is described. To a solution of sodium butylate, prepared by the reaction of 0.17 g of sodium with 10 ml of n-butanol (b. p. 117°), heated to 100° was added a mixture of solutions of 0.25 g of copper acetate in 40 ml of n-butyl alcohol and 0.7 g of dye (I) in 50 ml of toluene. The mixture obtained was heated for 2 hours at 100° with stirring and then 35 ml of 10% sulfuric acid (free from chlorine ions) was added and stirring continued for a further 10 minutes. The reaction mixture was carefully transferred to a separating funnel, diluted with 100 ml of benzene, and washed several times with distilled water (chlorine ions were absent from a control wash). The wash solutions were collected in a 500-ml measuring flask and diluted to the mark with distilled water, a sample taken with a 10-ml pipette, and the chlorine titrated potentiometrically with 0.01 N silver nitrate solution (with silver and calomel electrodes and a P-4 potentiometer). The consumption of 0.01 N $AgNO_3$ in parallel titrations was 4.98 and 4.97 ml and the average 4.975 ml, which corresponds to a chlorine ion content in the reaction mass (i.e., replaced chlorine) of 99.5% relative to the chlorine content of the starting dye (I).

The results of the other experiments are given in Table 2.

For isolation of the reaction products, the reaction mass after the chlorine ions had been washed out was dried with anhydrous sodium sulfate, evaporated in vacuum to 3-5 ml, and left overnight. The precipitate was collected, washed with a small amount of cold alcohol, and recrystallized from suitable solvents. The filtrate was evaporated to dryness in vacuum and the residue also purified by recrystallization. The total amounts of

TABLE 2

Reaction of Dyes with Sodium Butylate*

Starting dye			Reaction time (in hours)	0.01 N $AgNO_3$ consumed (in ml)	Chlorine replaced (in %)	Notes
No.	weight (in g)	solvent (in ml)				
(I)	0.7	Toluene (50)	2	4.98, 4.97	99.5	0.77 g (97%) of 2-butoxybenzeneazo-2'-naphthol isolated
(II)	0.7	Toluene (50)	8	–	–	approximately 0.7 g of starting dye isolated
(III)	0.7	Toluene (50)	8	–	–	approximately 0.7 g of starting dye isolated
(IV)	0.7	Toluene (50)	8	–	–	approximately 0.7 g of starting dye isolated
(V)	0.616	Toluene (50)	2	4.93, 4.95	98.8	0.7 g (100%) of 2-butoxy-5'-methyl-2'-hydroxyazobenzene isolated
(VI)	0.78	Chlorobenzene (50) + benzene (20)	8	–	–	approximately 0.78 g of starting dye isolated
(VI)	0.78	Pyridine (50)	8	–	–	approximately 0.78 g of starting dye isolated
(VI)	0.859	Pyridine (50)	8	–	–	Reaction with copper complex of dye (VI) without copper acetate
(VII)	0.79	Chlorobenzene (50)	8	3.35, 3.32	66.7	0.47 g (53%) of 2-butoxybenzeneazoacetoacetanilide isolated
(VIII)	0.7	Toluene (50)	8	1.05, 1.06	21.1	
(VIII)	0.78	Toluene (90)	8	1.07, 1.09	21.6	Reaction with copper complex of dye (VIII) without copper acetate
(IX)	0.74	Toluene (50)	8	0.32, 0.33	6.5	0.73 g (87%) of 1-chlorobenzeneazo-2'-butoxynaphthalene and 0.05 g (6.2%) of 2-butoxybenzeneazo-2'-naphthol isolated
(IX)	0.74	Toluene (50)	22	0.21, 0.28	5.7	0.73 g (87%) of 1-chlorobenzeneazo-2'-butoxynaphthalene and 0.05 g (6.2%) of 2-butoxybenzeneazo-2'-naphthol isolated
(X)	0.85		8	0.35, 0.37	7.2	

* The amounts of sodium, n-butyl alcohol, copper acetate, sulfuric acid, and benzene for dilution of the reaction mass and the capacities of the measuring flask and pipette were as in the experiment with dye (I) (see text).

products isolated are given in Table 2. The products were checked for chlorine content (Beilstein test) and identified; in experiments with dyes (II), (III), (IV), and (VI) and the copper complex of dye (VI) they were identified by mixed melting points with the corresponding starting dyes; in the experiment with dye (I), the product was identified by a mixed melting point with authentic butoxy-substituted dye.

In the experiment with dye (V), we obtained 0.7 g (100%) of the butoxy-substituted dye (2-butoxy-5'-methyl-2'-hydroxyazobenzene), which formed fine red needles with m. p. 83.5-84.0° after recrystallization from alcohol. Chlorine was absent.

Found %: N 9.73, 9.82. $C_{17}H_{20}O_2N_2$. Calculated %: N 9.85.

In the experiment with dye (VII) we obtained 0.47 g (53%) of the butoxy-substituted dye (2-butoxybenzeneazoacetoacetanilide) and after five recrystallizations from a mixture of methanol and benzene (2:1), it formed yellow needles with m. p. 146.7-147.3°. Chlorine was absent.

Found %: C 67.86, 68.10; H 6.62, 7.73; N 11.89, 11.81. $C_{20}H_{23}O_3N_3$. Calculated %: C 68.25; H 6.56; N 11.89.

In experiment with dye (IX), the reaction mixture was dried with sodium sulfate and evaporated almost to dryness in vacuum and 1 ml of methanol added to the viscous mass obtained. The substance then crystallized and the crystals were collected, washed with a small amount of methanol, and dried. The weight was 0.62 g. After recrystallization from methanol, the substance formed lustrous, dark cherry needles with m. p. 65.5-66.5°. The filtrate was evaporated to dryness and the remaining dark brown viscous mass (0.3 g) dissolved in benzene and chromatographed on alumina. We obtained 0.11 g of a substance which formed dark cherry needles with m. p. 64.5-65.5° and which did not depress the melting point of the main material, and a substance which formed fine red-orange needles with m. p. 115.5-117°, which did not depress the melting point of 2-butoxybenzeneazo-2'-naphthol. We obtained 0.05 g (6.2% of the starting 2-chlorobenzeneazo-2'-methoxynaphthalene) of 2-butoxybenzeneazo-2'-naphthalene.

The substance with m. p. 65.5-66.5° contained chlorine and was insoluble in aqueous caustic alkali. In elementary composition it corresponded to 2-chlorobenzeneazo-2'-butoxynaphthalene.

Found %: C 71.09, 71.01; H 5.52, 5.43; N 8.49, 8.38; Cl 10.15. $C_{20}H_{19}ON_2Cl$. Calculated %: C 70.89; H 5.65; N 8.26; Cl 10.46.

We obtained a total of 0.73 g (87% of the starting 2-chlorobenzeneazo-2'-methoxynaphthalene) of 2-chlorobenzeneazo-2'-butoxynaphthalene.

SUMMARY

1. We studied the reaction (in the presence of copper salts) of sodium n-butylate with chlorine-containing azo compounds, differing in the position of the chlorine atom and the electron-donor substituent relative to the azo group, and also in the nature of the electron-donor substituent.

2. It was established that replacement of the halogen atom in azo compounds occurs only when both the halogen atom and the electron-donor substituent are close (in the ortho position) to the azo group and when the electron-donor substituent contains a labile hydrogen atom; the reaction then occurs more readily, the more readily this hydrogen is replaced by metal.

3. It was shown that the halogen atom may be replaced in azo dyes with arilides of β-keto acids and amines as the azo component.

4. It was found that the halogen atom is replaced by an alkoxyl group during the reaction of the copper complex of an o-halo-o'-aminoazo dye with alcoholate in the absence of free copper salt.

5. It was found that when an azo dye containing a methoxyl group in the naphthalene nucleus ortho to the azo group is heated with sodium butylate in the presence of a copper salt, the methyl residue in the ether group is replaced by a butyl residue, i.e., there is transalkylation of the alkoxyl group.

LITERATURE CITED

1. I. M. Kogan, Chemistry of Dyes [in Russian] (1956), p. 170.
2. M. A. Andreeva and B. I. Stepanov, Zhur. Obshch. Khim. 28, 2966 (1958).*
3. B. I. Stepanov and V. A. Savel'ev, Zhur. Obshch. Khim. 28, 2968 (1956).*
4. Beilst. 16, 163.
5. A. I. Kizber and A. S. Glagoleva, Zhur. Obshch. Khim. 23, 1028 (1953).*
6. H. Singu, Sci. Papers Inst. Chem. Research (Tokyo) 35, 78 (1938); Chem. Abs. 33, 3369 (1939).
7. Color Index, 2nd Edition 3, 3036 (1956).
8. Beilst. 16, 1st Suppl., 328.
9. G. Charrier and G. Ferreri, Gazz. 42, II, 117 (1912).
10. G. B. Crippa, Gazz. 57, 497 (1927).
11. V. I. Mur, Zhur. Obshch. Khim. 25, 374 (1955).*
12. V. I. Mur, Zhur. Obshch. Khim. 24, 574 (1954).*

* Original Russian pagination. See C. B. translation.

SPECTRA AND HALOCHROMISM OF DI-(2-DIMETHYLAMINO-5-PYRIDYL)-METHANE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1356-1359, April, 1960
Original article submitted April 4, 1959

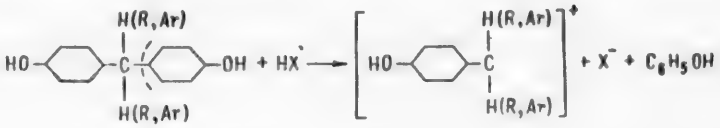
Di-(2-dimethylamino-5-pyridyl)-methane, whose synthesis was first described in [1], gives a red color with hot concentrated sulfuric acid [2]. The reason for the appearance of this color has not been studied by anyone, though the elucidation of the mechanism whereby it arises is undoubtedly of interest.

It is now well-known [3-5] that the appearance of color during the solution of colorless aromatic carbinols in concentrated sulfuric acid is connected with the formation of carbonium salts, the cation of which is the color carrier.

$$(C_6H_5)_3COH + 2H_2SO_4 \rightleftarrows [(C_6H_5)_3C]^+ + 2HSO_4^- + H_3O^+$$

The literature contains more than one report of the appearance of color during the solution of some aromatic derivatives of methane in concentrated sulfuric acid [6-9].

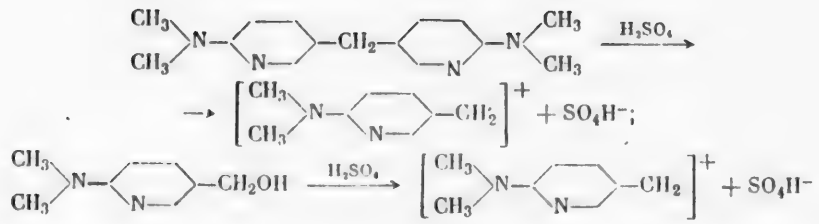
As a result of our investigations [10-12] it was possible to establish that the reaction between aromatic derivatives of methane and strong protonic acids also proceeds by a type of acid-base interaction, causing the formation of corresponding carbonium salts.



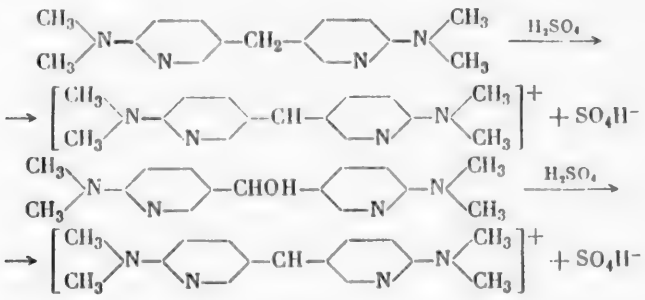
The appearance of color during the solution of di-(2-dimethylamino-5-pyridyl)-methane in hot concentrated sulfuric acid and, as we established, its disappearance on dilution with water indicate the halochromic nature of this phenomenon, i.e., the formation of a carbonium salt. As follows from the data presented above for aromatic derivatives, the formation of a carbonium salt from the given heterocyclic compound may proceed in two possible directions. According to one of these, the carbonium salt may form due to cleavage of molecules of the heterocyclic derivative at the methane bond. The second direction may be connected with oxidation of this compound to corresponding carbinol and subsequent salt formation. To determine the actual reason for color formation, we undertook a spectrophotometric investigation of this phenomenon.

In the formation of a carbonium salt in the first direction, there should be similarity between the absorption curves of sulfuric acid solutions of di-(2-dimethylamino-5-pyridyl)-methane and 2-dimethylamino-5-pyridylcarbinol.*

* In order to simplify the interpretation of the basic process, in describing the reactions we omit salt formation at the nitrogen atoms.



With the process going in the second direction, a similar picture should be obtained with the absorption curve of a sulfuric acid solution of di-(2-dimethylamino-5-pyridyl)-carbinol.



By measuring the absorption spectra of alcohol and sulfuric acid solutions of 2-dimethylamino-5-pyridylcarbinol, di-(dimethylamino-5-pyridyl)-carbinol, and di-(2-dimethylamino-5-pyridyl)-methane it was found that the absorption spectrum of an acid solution of the first compound (Fig. 1) differed little from that in alcohol, while for the second compound (Fig. 2), there was a considerable difference between the curves of acid and alcohol solutions. A similar substantial difference was observed between the curves of the heterocyclic derivative of methane (Fig. 3).

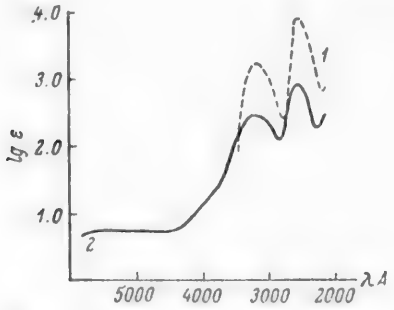


Fig. 1. Absorption spectra of 2-dimethylamino-5-pyridylcarbinol. 1) In C_2H_5OH; 2) in concentrated H_2SO_4.

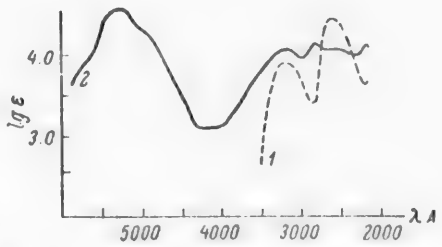
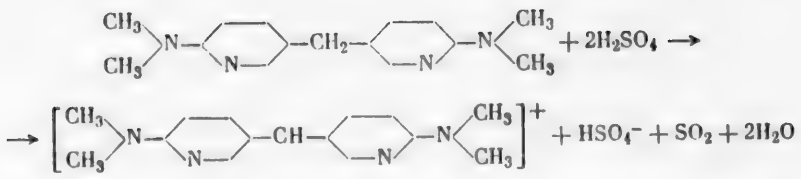


Fig. 2. Absorption spectra of di-(2-dimethylamino-5-pyridyl)-carbinol. 1) In C_2H_5OH; 2) in concentrated H_2SO_4.

On comparing the absorption curves of acid solutions of all these compounds, we see (Fig. 4) that 2-dimethylamino-5-pyridylcarbinol does not have selective absorption in the visible region of the spectrum. In this region of the spectrum, di-(2-dimethylamino-5-pyridyl)-carbinol and di-(2-dimethylamino-5-pyridyl)-methane have well-expressed absorption bands with identical values of λ_{max}, but different intensities.

From these data it follows that the appearance of color in a hot sulfuric acid solution of di-(2-dimethylamino-5-pyridyl)-methane is not connected with cleavage of its molecule, but is the result of oxidation and the formation of the corresponding dipyridylcarbonium salt.



Simple calculation from the value of ε of the absorption band maxima in the visible part of the spectrum showed that about 2% of the total amount of dissolved di-(2-dimethylamino-5-pyridyl)-methane was oxidized in this solution.

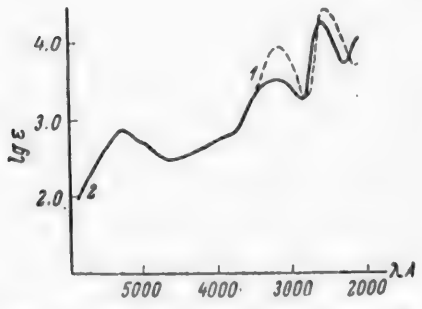


Fig. 3. Absorption spectra of di-(2-dimethylamino-5-pyridyl)-methane. 1) In C_2H_5OH; 2) in concentrated H_2SO_4.

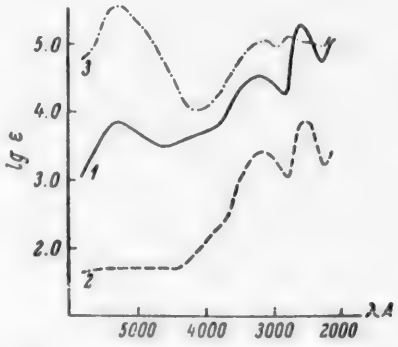


Fig. 4. Absorption spectra in concentrated H_2SO_4. 1) Di-(2-dimethylamino-5-pyridyl)-methane; 2) 2-dimethylamino-5-pyridylcarbinol; 3) di-(2-dimethylamino-5-pyridyl)-carbinol.

In our opinion, cleavage of a C – C bond did not occur because salt formation at all the nitrogen atoms of di-(2-dimethylamino-5-pyridyl)-methane considerably weakens the basicity of the methane carbon, which plays a decisive role in this direction of acid--base interaction [10-12].

The compounds needed for this investigation were synthesized and purified by methods described in the literature [2, 13, 14].

SUMMARY

1. A spectrophotometric investigation was made of alcohol and sulfuric acid solutions of 2-dimethylamino-5-pyridylcarbinol, di-(2-dimethylamino-5-pyridyl)-carbinol, and di-(2-dimethylamino-5-pyridyl)-methane.

2. From the absorption spectra of acid solutions of these compounds it was established that the appearance of the red color during the solution of di-(2-dimethylamino-5-pyridyl)-methane in hot sulfuric acid is connected with the formation of the corresponding dipyridylcarbonium salt.

LITERATURE CITED

1. A. Chichibabin and I. Knunyants, Ber. 62, 3048 (1929).
2. I. L. Knunyants and V. M. Berezovskii, Synthetic Organic Preparations [in Russian] (1950), Vol. 1, p. 49.
3. L. P. Hammett and A. J. Deyrup, J. Am. Chem. Soc. 55, 1900 (1933).
4. L. P. Hammett, Physical Organic Chemistry (New Jersey, 1940), p. 54.
5. V. F. Lavrushin, Zhur. Obshch. Khim. 26, 2697 (1956).*
6. E. ter Meer, Ber. 7, 1200 (1874).

* Original Russian pagination. See C. B. translation.

7. A. Dianin, Zhur. Russ. Fiz. Khim. Obshchest. 23, 488 (1891).
8. A. Bayer and V. Villiger, Ber. 35, 1189 (1902).
9. D. Boyd and D. Hardy, J. Chem. Soc. (1928), p. 630.
10. V. F. Lavrushin, Izvest. Akad. Nauk SSSR, Otdel. Fiz. Nauk 17, 723 (1953).
11. V. F. Lavrushin, Doklady Akad. Nauk SSSR 86, 309 (1952).
12. V. F. Lavrushin, Doklady Akad. Nauk SSSR 95, 809 (1954).
13. A. I. Titov and A. N. Baryshnikova, Zhur. Obshch. Khim. 23, 293 (1953).*
14. I. L. Knunyants and V. M. Berezovskii, Zhur. Obshch. Khim. 18, 779 (1948).

* Original Russian pagination. See C. B. translation.

SPECTRA AND HALOCHROMISM OF SOME UNSATURATED ALIPHATIC ALCOHOLS

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In a series of papers [1-3] we reported a study of the spectra and halochromism of saturated alicyclic and aliphatic alcohols. It was established that these compounds give colored solutions with concentrated sulfuric acid, which are decolorized by dilution with water. A study of the absorption spectra of their sulfuric acid solutions showed that they have similar absorption curves with an intense band in the region of 3000 A and a long-wave inflection extending into the visible part of the spectrum.

The literature contains reports of only a few cases of the appearance of color during the reaction of some unsaturated alcohols with acids [4-6]. We undertook a study of the behavior toward various acids of olefinic alcohols with the double bond conjugated with the carbinol function and also a study of the absorption spectra of their acid solutions. For this purpose, we prepared 2-methylpenten-2-ol-4, 2,4-dimethylhexen-2-ol-4, and 2-methyl-3-ethylpenten-1-ol-3.

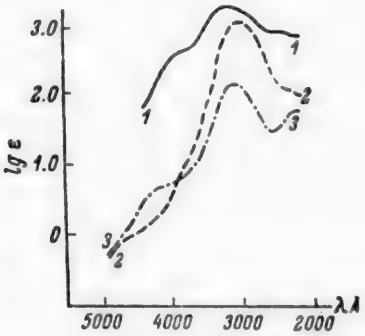

Fig. 1. Absorption spectra. In concentrated H_2SO_4: 1) 2-methylpenten-2-ol-4; 2) 2,4-dimethylhexen-2-ol-4; 3) 2-methyl-3-ethylpenten-1-ol-3.

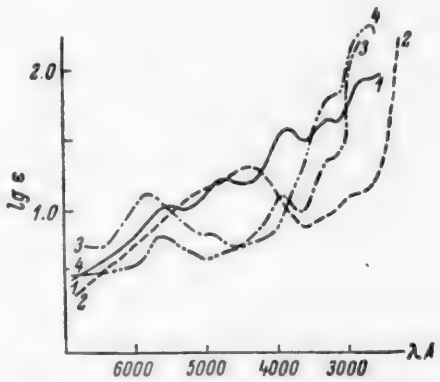

Fig. 2. Absorption spectra of 2-methylpenten-2-ol-4. 1) 30% H_2SO_4 in CH_3COOH; 2) 20% HCl in C_2H_5OH; 3) 90% CCl_3COOH; 4) 30% H_3PO_4 in CH_3COOH.

When all these olefinic alcohols were dissolved in concentrated sulfuric acid, a yellow-orange color appeared immediately and this disappeared on dilution with alcohol or water. A study of their behavior toward other acids showed that these alcohols, in contrast to saturated tertiary alcohols, readily form colored solutions in sulfuric and phosphoric acids diluted with glacial acetic acid, in an alcohol solution of hydrogen chloride, and in trichloroacetic acid. The yellow-orange color thus produced rapidly deepened very strongly. Dilution of all these solutions with alcohol or water also led to disappearance of the color.

Measurement of the absorption spectra of acid solutions of olefinic alcohols led us to extremely interesting results. First, it was found that concentrated sulfuric acid solutions of all the alcohols gave the same type of absorption as saturated alicyclic and aliphatic alcohols with a band in the middle ultraviolet region and an inflection in the visible part of the spectrum (Fig. 1). Secondly, it was found that the light absorption by solutions of these alcohols in other acids is extremely complex (Figs. 2-4). As the figures presented show, in addition to the absorption band in the middle ultraviolet region, the curves of dilute sulfuric acid solutions showed a further series of more or less clearly expressed bands. Almost all these bands were repeated on the absorption curves of the other acid solutions.

The difference in the absorption spectra of solutions of olefinic alcohols in concentrated sulfuric acid and dilute acids is undoubtedly connected with the different nature of the reaction between the acids and the alcohols.

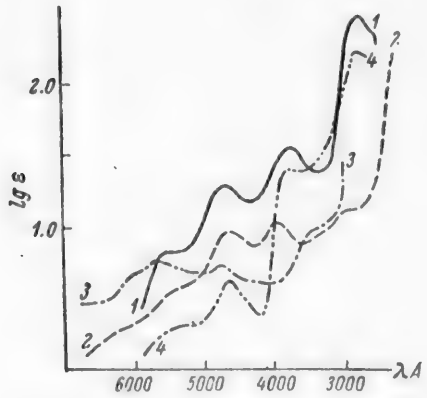

Fig. 3. Absorption spectra of 2,4-dimethylhexen-2-ol-4. 1) 30% H_2SO_4 in CH_3COOH; 2) 20% HCl in C_2H_5OH; 3) 90% CCl_3COOH; 4) 30% H_3PO_4 in CH_3COOH.

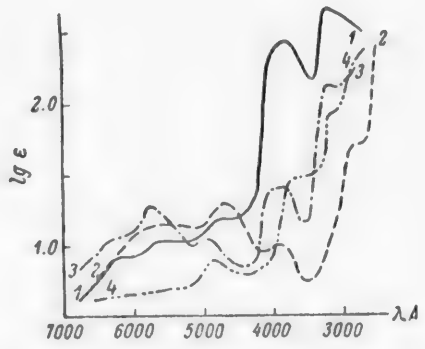

Fig. 4. Absorption spectra of 2-methyl-3-ethylpenten-1-ol-3. 1) 30% H_2SO_4 in CH_3COOH; 2) 20% HCl in C_2H_5OH; 3) 90% CCl_3COOH; 4) 30% H_3PO_4 in CH_3COOH.

Since unsaturated alcohols in concentrated sulfuric acid give the same type of absorption as saturated tertiary alcohols and diisobutylene [1-3], it can be assumed that in this case there are simultaneously an acid–base interaction at the carbinol function and protonization of the double bond, resulting in the formation of dicarbonium ions, for example:

$$CH_3-\underset{\displaystyle CH_3}{\overset{}{C}}=CH-\overset{\displaystyle OH}{\overset{|}{\underset{\displaystyle CH_3}{\overset{|}{C}}}}-C_2H_5 + 2H_2SO_4 \longrightarrow \left[CH_3-\underset{\displaystyle CH_3}{\overset{}{C}}-CH_2-\underset{\displaystyle CH_3}{\overset{}{C}}-C_2H_5\right]^{++} + 2HSO_4^- + H_2O.$$

As we established, saturated tertiary alcohols and diisobutylene do not give any color with dilute sulfuric acid or the other dilute acids used in the present investigation. Nonetheless, all our unsaturated alcohols formed deeply colored solutions under these conditions. It is probable that in these alcohols the basicity of the carbinol group is considerably increased by the action of the radicals with a double bond and therefore the acid–base interaction with dilute and weaker acids becomes possible, for example:

$$CH_3-\underset{\displaystyle CH_3}{\overset{}{C}}=CH-\overset{\displaystyle OH}{\overset{|}{\underset{\displaystyle CH_3}{\overset{|}{C}}}}-C_2H_5 + HX \longrightarrow \left[CH_3-\underset{\displaystyle CH_3}{\overset{}{C}}=CH-\underset{\displaystyle CH_3}{\overset{}{C}}-C_2H_5\right]^{+} + X^- + H_2O$$

Since the double bond is not touched in this process, the appearance of a positive charge on the carbon atom produces strong conjugation with the olefinic radical. The formation of a conjugated carbonium cation is apparently

the reason for such deep coloration of dilute acid solutions. Thus, in our opinion, the two types of absorption spectra observed in the investigation for solutions of unsaturated alcohols in concentrated sulfuric acid and in dilute acids is caused by the different structure of the cations formed during the reaction of alcohols with acids.

The unsaturated alcohols required for the investigation were synthesized and purified by methods described in the literature [7-9]. The absorption spectra were measured on a nonrecording SF-4 spectrophotometer and on a recording SF-2m spectrophotometer.

SUMMARY

1. We studied the absorption spectra of solutions of 2-methylpenten-2-ol-4, 2,4-dimethylhexen-2-ol-4, and 2-methyl-3-ethylpenten-1-ol-3 in concentrated sulfuric acid, in sulfuric and phosphoric acids diluted with glacial acetic acid, in an alcohol solution of hydrogen chloride, and in trichloroacetic acid.

2. It was established that all the unsaturated alcohols studied give two types of absorption spectra in concentrated acid and in dilute acids.

3. It is proposed that the two types of absorption spectra observed for solutions of unsaturated alcohols in different acids are caused by the different structure of the cations of the carbonium salts formed.

LITERATURE CITED

1. V. F. Lavrushin, N. N. Verkhovod, and P. K. Movchan, Doklady Akad. Nauk SSSR 105, 723 (1955).
2. V. F. Lavrushin and N. N. Verkhovod, Zhur. Obshch. Khim. 26, 2704 (1956).*
3. V. F. Lavrushin and N. N. Verkhovod, Doklady Akad. Nauk SSSR 115, 312 (1957).*
4. C. Prevost, Compt. rend. 195, 1032 (1932).
5. B. N. Dashkevich, I. V. Smolanka, and Yu. Yu. Tsmur, Nauchn. Zap. Uzhgor. GU 22, 92 (1957).
6. B. N. Dashkevich and Yu. Yu. Tsmur, Eighth Mendeleev Conference, Organic Chemistry and Technology Section [in Russian] (Izd. AN SSSR, 1959), p. 301.
7. H. Lund, Ber. 70, 1525 (1937).
8. Pastureau and H. Bernard, Compt. rend. 179, 183 (1924).
9. E. E. Blaise and A. Courtot, Compt. rend. 140, 372 (1905).

* Original Russian pagination. See C. B. translation.

DIRECT AMINATION OF BENZTHIAZOLE DERIVATIVES

II. AMINATION OF NITROBENZTHIAZOLES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 4, pp. 1363-1366, April, 1960
Original article submitted April 13, 1959

In a previous communication [1] it was shown that when treated with hydroxylamine, 5-methyl-, 5-amino-, and 5-carboxybenzthiazoles form the corresponding 2-amino derivatives. The reaction was carried out in an aqueous medium with the equivalent amount of hydroxylamine or a molar excess of it [2]. 5-Nitrobenzthiazole did not react under these conditions.

In the amination of 6-nitrobenzthiazole with a large excess of hydroxylamine (10 moles per mole of nitrobenzthiazole) in alcohol, a quantitative yield of 2-amino-6-nitrobenzthiazole was obtained [3].

By using the reaction conditions reported by the authors for the amination of isomeric nitrobenzthiazoles, we obtained 2-amino-6-nitrobenzthiazole in 91% yield, 2-amino-5-nitrobenzthiazole in 54% yield, and 2-amino-4-nitrobenzthiazole in 23% yield. 7-Nitrobenzthiazole could not be aminated; when the reaction was carried out in 96% alcohol, the starting 7-nitrobenzthiazole was recovered, while if diluted alcohol was used, in addition to 7-nitrobenzthiazole, we isolated an amino product with a low melting point, which was apparently 7-aminobenzthiazole. The yield of the latter was insignificant.

The starting 5-nitrobenzthiazole was obtained from 1-formylamino-2-bromo-5-nitrobenzene. The remaining isomers of nitrobenzthiazole were obtained by nitration of benzthiazole with a mixture of nitric and sulfuric acids [4].

By a study of the effect of different temperatures on the nitration of benzthiazole it was shown that in addition to the main reaction product, namely, 6-nitrobenzthiazole, 7-nitrobenzthiazole was formed [5]. It was also found that at 0°, 62% of 6-nitrobenzthiazole with m. p. 170-172° and 9.1% of 7-nitrobenzthiazole with m. p. 150-154° were formed [6].

Then it has been reported that the nitration of benzthiazole at 35° gives 4-nitrobenzthiazole (m. p. 135°) in addition to 6-nitrobenzthiazole (m. p. 174°) [7]. The structure of the isomers obtained was not demonstrated satisfactorily in any of the papers mentioned.

We carried out the nitration at 6-8° and at 15-25°. The total yield of nitration products was 85-91%. Individual isomers were isolated from this mixture by repeated recrystallization from methanol, ethanol, benzene, and water (see Table 1).

In addition, at 15-25° we obtained a small amount of polynitro compound with m. p. 190°, which we did not investigate.

For a more precise determination of the position of the nitro group, we determined the ultraviolet absorption spectra of these compounds and compared them with those of 2-methylnitrobenzthiazoles, whose structures have been determined unequivocally [8]. The data obtained are presented in Table 2.

TABLE 1

Nitration Products of Benzthiazole (at 6-8°)

Isomer	Yield (in %)	Melting point	Formula	%, N	
				found	calculated
4-Nitrobenzthiazole	13	105-106°	$C_7H_4O_2N_2S$	15.05, 14.87	15.12
6-Nitrobenzthiazole	50	174°			
7-Nitrobenzthiazole	7	153-154°	$C_7H_4O_2N_2S$	15.13, 14.96	15.12

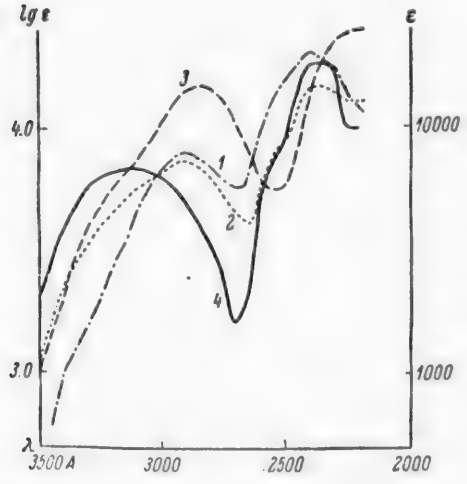
TABLE 2

Ultraviolet Absorption Maxima of Nitrobenzthiazoles and 2-Methylnitrobenzthiazoles

Nitro derivatives of benzthiazole	λ_{max}		Nitro derivatives of 2-methylbenzthiazole*
4-Nitrobenzthiazole (m. p. 105°)	292	298	4-Nitro-2-methylbenzthiazole
5-Nitrobenzthiazole	290	292	5-Nitro-2-methylbenzthiazole
6-Nitrobenzthiazole	285	293	6-Nitro-2-methylbenzthiazole
7-Nitrobenzthiazole (m. p. 154°)	310	308	7-Nitro-2-methylbenzthiazole

* Data of E. D. Sych (private communication).

As the data presented in Table 2 show, the absorption maximum of the nitrobenzthiazole with m. p. 154° is considerably displaced toward long wavelengths, as occurs with 2-methyl-7-nitrobenzthiazole; this compound is apparently 7-nitrobenzthiazole. Consequently, the compound with m. p. 105° is 4-nitrobenzthiazole. The ultraviolet absorption curves of nitrobenzthiazoles are given in the figure.



Ultraviolet absorption curves. 1) 4-Nitrobenzthiazole; 2) 5-nitrobenzthiazole; 3) 6-nitrobenzthiazole; 4) 7-nitrobenzthiazole.

The reduction of 4- and 7-nitrobenzthiazoles with stannous chloride in hydrochloric acid yielded 4-amino-benzthiazole with m. p. 122° (from water) and 7-aminobenzthiazole with m. p. 123° (from water) [5]. Their acetyl derivatives were prepared (melting points 160 and 178°, respectively).

EXPERIMENTAL

Nitration of benzthiazole. Into a three-necked flask fitted with a mechanical stirrer, dropping funnel, and thermometer was placed 156 ml of concentrated sulfuric acid. With external cooling and stirring, 78 g of benzthiazole (obtained by treating 2-mercaptobenzthiazole with hydrogen peroxide) [9] was added and then 78 ml of fuming nitric acid (d 1.5) was introduced dropwise at such a rate that the temperature of the reaction mixture was 6-8° (the addition required 2 hours). When the nitric acid had been added, the reaction mass was kept at 8° for 2 hours and then poured into ice water. After 15-20 minutes, the pale yellow, curdy precipitate was collected, washed with water, and dried in air. The nitration product yield was 88 g (85 %) and the m. p. 95-151°. For separation of the mixture of nitrobenzthiazole isomers, the product was boiled with 10 times the amount of methanol and the mixture filtered hot. The bulk of the 6-nitrobenzthiazole remained undissolved. Recrystallization from a large volume of methanol or ethanol yielded pure 6-nitrobenzthiazole with m. p. 174°.

On cooling, the methanol solution deposited a mixture of isomers and repeated recrystallization of this from methanol, ethanol, and benzene yielded some more 6-nitrobenzthiazole, 7-nitrobenzthiazole (m. p. 153-154°), and a little 4-nitrobenzthiazole (m. p. 105-106°). After evaporation of the methanol mother liquor to small volume, the bulk of the 4-nitrobenzthiazole separated as a pale yellow, low-melting substance. It was extracted with boiling water and recrystallized from aqueous alcohol. The yield of purified isomers was 50% of 6-nitrobenzthiazole, 13% of 4-nitrobenzthiazole, and 7% of 7-nitrobenzthiazole.

4-Nitrobenzthiazole formed pale yellow needles from water. It was soluble in methanol, ethanol, benzene, and hot water and sparingly soluble in cold water. When treated with stannous chloride in hydrochloric acid it was converted to 4-aminobenzthiazole, which formed coarse, colorless needles with m. p. 122°. The acetyl derivative was obtained by heating a benzene solution of the amine with acetic anhydride. The colorless needles (from water) had m. p. 158-160°.

7-Nitrobenzthiazole formed yellow needles (from water or alcohol). It was soluble in ether, hot methanol, hot ethanol, and hot benzene and sparingly soluble in water. It was reduced by stannous chloride to 7-aminobenzthiazole, which formed colorless, feathery needles (from water) with m. p. 123°. The acetyl derivative formed colorless needles (from water) with m. p. 178°.

Amination of 6-nitrobenzthiazole [3]. Into a three-necked flask fitted with a mechanical stirrer, thermometer, dropping funnel, and reflux condenser was placed a carefully ground mixture of 1 g of 6-nitrobenzthiazole, 5 g of hydroxylamine hydrochloride, and 50 ml of alcohol, the mixture heated to 50° on a water bath, and a solution of 5 g of potassium hydroxide in 35 ml of alcohol added dropwise with stirring over a period of 35 minutes. The reaction mixture was stirred at 48-52° for 2 hours. A colorless, crystalline precipitate (KCl) formed. The cooled reaction mixture was poured into 400 ml of cold water. A precipitate separated after a short time. It was collected, washed with water, and dried at 70°. We obtained 0.3 g of lemon yellow needles with m. p. 250-251°. Evaporation of the mother liquor to 200 ml yielded a further 0.68 g of product. The total yield was 0.98 g (91%). A mixed melting point with 2-amino-6-nitrobenzthiazole, obtained by cyclization of p-nitrophenylthiourea, was not depressed.

If sodium ethylate (from 1.9 g of metallic sodium) was used instead of potassium hydroxide, the yield of product with m. p. 252° was 74%.

Amination of 4-nitrobenzthiazole. In the apparatus described above were heated 0.8 g of 4-nitrobenzthiazole, 4 g of hydroxylamine hydrochloride, and 30 ml of alcohol and then 4 g of potassium hydroxide in 40 ml of alcohol was added dropwise over a period of 25 minutes. The reaction mixture was stirred at 52-60° for a further 3 hours. The cooled mixture was filtered to remove the potassium chloride precipitate, the filtrate evaporated to 20 ml and then diluted with water (1 : 3). After 16 hours, the yellow precipitate was collected, washed with water, and recrystallized from n-butanol to give fine yellow needles with m. p. 234-235° (232° [10] and 254° [11]). The yield was 0.2 g (23%). The product was soluble in glacial acetic acid and hot n-butanol and insoluble in water, ethanol, and methanol. It was diazotized in concentrated hydrochloric acid.

Found %: N 21.74, 21.85. $C_7H_5O_2N_3S$. Calculated %: N 21.53.

Amination of 5-nitrobenzthiazole. 5-Nitrobenzthiazole was aminated under the conditions described above (see amination of 4-nitrobenzthiazole). We obtained a brownish yellow substance in 54% yield and this had decomp. p. about 270°. After recrystallization from aqueous pyridine, the product formed lemon yellow needles with decomp. p. 308-309°. It was soluble in chloroform, n-butanol, and pyridine, insoluble in water and benzene, and sparingly soluble in alcohol. It was diazotized in concentrated hydrochloric acid.

Found %: N 21.40, 21.43. $C_7H_5O_2N_3S$. Calculated %: N 21.53.

Amination of 7-nitrobenzthiazole. 7-Nitrobenzthiazole was aminated as described above; the starting 7-nitrobenzthiazole was recovered in 90% yield.

If an aqueous solution of hydroxylamine hydrochloride was added to an alcohol solution of 7-nitrobenzthiazole and then an aqueous solution of alkali and the reaction mixture boiled under reflux for 4 hours (boiling point 82°), we obtained a mixture of substances with m. p. 136-147° in 75% yield. Recrystallization from alcohol yielded the starting 7-nitrobenzthiazole (about 45%) and an insignificant amount of colorless needles with a m. p. below 100°, which could not be investigated. It is possible that this was 7-aminobenzthiazole.

SUMMARY

1. The nitration of benzthiazole with a mixture of nitric and sulfuric acids at 6-8° and 15-25° gave 6-nitrobenzthiazole (50% yield), 4-nitrobenzthiazole (13% yield), and 7-nitrobenzthiazole (7% yield).

The position of the nitro group in the isomeric nitrobenzthiazoles was established by comparison of their ultraviolet absorption spectra with those of 2-methylnitrobenzthiazoles of established structure.

2. The action of hydroxylamine in alcohol on nitrobenzthiazoles formed the corresponding 2-amino-nitrobenzthiazoles. 6-Nitrobenzthiazole was aminated most readily (91% yield); the other isomers reacted with more difficulty and the yield of 2-amino-4-nitrobenzthiazole was 23% and that of 2-amino-5-nitrobenzthiazole was 54%, while 2-amino-7-nitrobenzthiazole could not be obtained under the given conditions.

LITERATURE CITED

1. R. P. Vel'tman, Zhur. Obshch. Khim. 26, 3388 (1956).*
2. A. Skraup, Lieb. Ann. 419, 13 (1919).
3. M. Kolonna and F. Montanari, Gazz. 81, 744 (1951).
4. W. Boggust and W. Cocker, J. Chem. Soc. (1949), p. 355.
5. H. Nishizawa, J. Pharm. Soc. 62, 47 (1942); Chem. Abs. 45, 609 (1951).
6. J. Mizuno, K. Adachi, and K. Nakamura, J. Pharm. Soc. 72, 1266 (1952); Chem. Abs. 47, 12,357 (1953).
7. P. Petitcolas, R. Sureau, J. Frenkiel, and R. Goupil, Bull. Soc. Chim. (1949), p. 103.
8. E. D. Sych, Ukr. Khim. Zhur. 14, 107 (1949).
9. U. S. Patent 2,509,453; Chem. Abs. 44, 7885 (1950).
10. G. Dyson, R. Hunter, and R. Morris, J. Chem. Soc. (1927), 1186.
11. H. Erlenmeyer and H. Ueberwasser, Helv. Chim. Acta 23, 328 (1940).

* Original Russian pagination. See C. B. translation.

PERFUMES FROM ALKYLPHENOLS

I. SYNTHESIS OF PERFUMES FROM DIMETHYLPHENYL-p-CRESOL

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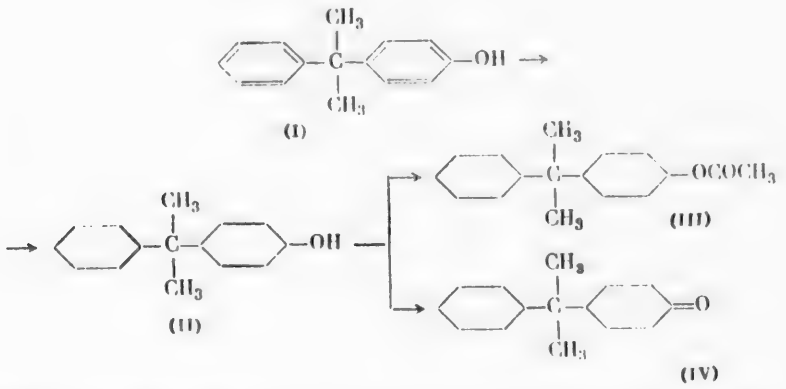
Certain alkylphenols [1] and terpenylphenols [2-9] recently have found application as intermediates in the synthesis of perfumes; therefore, it appeared interesting to attempt such utilization of a newly available product, 2-(p-hydroxyphenyl)-2-phenylpropane (I), produced in large quantities in the chemical industry under the name "dimethylphenyl-p-cresol."

Judging by the available information [1-9], the synthesis of perfumes from alkylphenols is possible only after converting them to the corresponding substituted cyclohexanols, cyclohexyl acetates, or cyclohexanones; therefore, we subjected the phenol (I) to the corresponding conversions [10].



The hydrogenation of (I) with skeletal nickel catalyst was carried out to the theoretical absorption of hydrogen for both aromatic rings; the completeness of hydrogenation was confirmed by the absence of absorption in the UV spectrum, which would necessarily be observed if aromatic compounds remained in the reaction product [see spectrum of the initial material (I) on p. 1399].

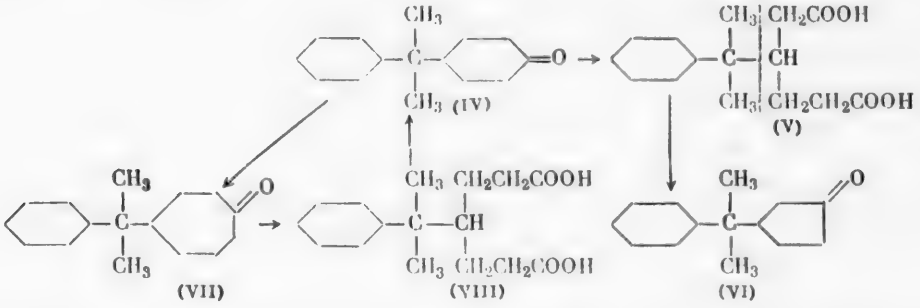
The hydrogenated product, 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane (II), is an extremely viscous colorless liquid with practically no odor. The acetate of this alcohol (III), a colorless transparent liquid, is considerably less viscous than the original alcohol; in contrast to the acetate of p-tert-butylcyclohexanol, which has a strong floral odor, the acetate (III) has only a faint noncharacteristic odor and is thus similar to the acetates of menthylcyclohexanol and bornylcyclohexanol which were described earlier [7].

Oxidation of the alcohol (II) by chromate mixture in acetic acid gives a high yield of 2-(4'-ketocyclohexyl)-2-cyclohexylpropane (IV).

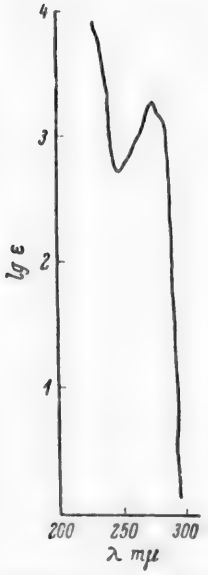
Transition from the alcohol to the ketone is accompanied by intensification of odor as expected; the ketone (IV) has a pronounced distinctive odor of the same character as that of p-tert-butylcyclohexanone [1], but weaker. This relatively weaker odor apparently is explained by the greater molecular weight of (IV); however, this does not imply that the odor of substituted cyclohexanones depends solely upon the size of the substituent regardless of its structure, since almost all terpenylcyclohexanones (which have still heavier substituents) possess strong and stable odors [7].

For the purpose of obtaining new data on the relationship between the structure of cyclic ketones and their odor, it appeared interesting to study the effect of change of ring size upon odor.

Therefore, we carried out the contraction of the cyclohexanone ring of the ketone (IV) to cyclopentanone and its enlargement to cycloheptanone.



Contraction of the cyclohexanone ring of the ketone (IV) was accomplished by oxidizing the cyclohexanol (II) with nitric acid containing ammonium vanadate according to a method described earlier [11]. The 4-(1'-methyl-1'-cyclohexylethyl)-adipic acid (V), formed as a thick brown oil, is decomposed upon vacuum distillation. Therefore, it was purified by conversion to the dimethyl ester, from which (after vacuum distillation and saponification) the pure crystalline acid (V) was obtained successfully.



UV absorption spectrum of 2-(p-hydroxyphenyl)-2-phenylpropane (I).

Cyclization of (V) in the presence of $Ba(OH)_2$ at 200-350° [12] led to a mixture of hydrocarbons instead of the expected 2-(3'-ketocyclopentyl)-2-cyclohexylpropane (VI); the hydrocarbons were very likely formed by pyrolytic splitting of (V) at the place indicated by the dotted line. The same result was obtained by heating (V) to 200-350° without $Ba(OH)_2$. The mixture of hydrocarbons most probably consists largely of hexahydrocumene (isolated in sufficiently pure form by chromatographic separation of the mixture on silica gel) and also of various tetrahydrocumenes and a small amount of cumene.

The cyclopentanone derivative (VI), a strong-smelling liquid, was obtained in satisfactory yield by heating the acid (V) under vacuum at a temperature not over 200°.

For ring enlargement of the ketone (IV), we applied the recently suggested N-nitroso-N-methyl-p-toluenesulfamide [13], which has a number of important advantages over diazomethane and which has been used successfully in recent years for ring enlargement of cyclic ketones [14, 15].

The cycloheptanone derivative thus obtained, 2-(4'-ketocycloheptyl)-2-cyclohexylpropane (VII), is a crystalline substance with a faint odor. For proof of the cycloheptanone structure, (VII) was oxidized to 4-(1'-methyl-1'-cyclohexylethyl)-pimelic acid (VIII); upon cyclization of (VIII) the ketone (IV) was obtained again.

The nature of the odor is essentially unchanged upon transition from (IV) to (VI) and (VII); however, the contraction of the six-membered ketonic ring to a five-membered ring causes a marked strengthening of odor, whereas enlargement to a seven-membered ring causes a significant weakening of odor.

EXPERIMENTAL

1. Hydrogenation of 2-(p-hydroxyphenyl)-2-phenylpropane (I). Hydrogenation of 100 g of (I) (m. p. 72°) was carried out under 130 atm pressure at 120-170° with 10 g of skeletal nickel and 10 ml of alcohol. The hydrogen absorption over 3 hours was 67 liters (103%). Upon cooling, the hydrogenated product was dissolved in alcohol and filtered; after distilling off the alcohol, the product was vacuum distilled. The yield was 90 g (90%) of a product with b. p. 165-180° (4 mm) and content of 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane (II) approximately 100% (determined by acetylation).

The fraction taken for analysis had b. p. 165-170° (4 mm), d^{20}_4 0.9818, $n^{20}D$ 1.5104, MR_D 68.38; Calc. 68.58.

Found %: C 80.69, 80.50; H 12.86, 12.89. $C_{15}H_{28}O$. Calculated %: C 80.29; H 12.57.

3,5-Dinitrobenzoate, light yellow square plates, m. p. 161-162° (from methanol-chloroform, 3:1 by volume).

Found %: C 63.52, 63.23; H 7.35, 7.31; N 6.74, 6.89. $C_{22}H_{30}O_6N_2$. Calculated %: C 63.14; H 7.22; N 6.69.

2. Acetylation of 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane. To a mixture of 15 g of (II) and 45.5 g of acetic anhydride was added 5 g of a mixture of acetic anhydride and phosphoric acid (prepared at least 1 day ahead from 90 g of acetic anhydride and 10 g of concentrated phosphoric acid [16]). A considerable amount of heat was evolved. After a day the mixture was diluted with water; 2 hours later the water layer was drawn off and the oil was dissolved in benzene, washed with 5% sodium carbonate solution and with water, and dried with anhydrous sodium sulfate. After distilling off the benzene, the residue (22.5 g) was vacuum distilled. The yield of acetate was 17.4 g (73%) with ester content 99.5%, b. p. 193-196° (8 mm), d^{20}_4 0.9885, $n^{20}D$ 1.4890, MR_D 77.78; calc. 77.96. A redistilled fraction boiling at 146° (2 mm) crystallized upon standing, forming colorless plates, m. p. 58-59° (from alcohol).

Found %: C 76.65, 76.54; H 11.44, 11.39. $C_{17}H_{30}O_2$. Calculated %: C 76.62; H 11.42.

3. Oxidation of 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane. A solution of 51 g of $Na_2Cr_2O_7 \cdot 2H_2O$ in 135 g of 50% sulfuric acid was added with stirring over a 1-hour period to 90 g of (II) in 200 ml of glacial acetic acid and 20 ml of water, cooling as necessary to remain below 40°. Subsequently the reaction mixture was stirred for 1 hour at 30° and 1 hour at 70°, after which it was diluted with water. The crystalline product, 2-(4'-ketocyclohexyl)-2-cyclohexylpropane (IV) was filtered off and washed with sodium carbonate solution and with water. The yield was 85 g (95%) of ketone, which after steam distillation appeared as colorless thin needles, m. p. 86-87° (from alcohol-water), ketone content 99.9% (determined by oxime formation).

Found %: C 81.23, 81.29; H 12.21, 12.19. $C_{15}H_{26}O$. Calculated %: C 81.01; H 11.78.

Oxime, colorless rod-like crystals, m. p. 144° (from alcohol-water).

Found %: N 5.94, 6.10. $C_{15}H_{27}ON$. Calculated %: N 5.90.

2,4-Dinitrophenylhydrazone, small yellow crystals, m. p. 147-148° (from mixture of alcohol and ethyl acetate); λ max (in CH_3OH) 366 mμ (log ϵ 4.37).

Found %: N 13.72, 13.89. $C_{21}H_{30}O_4N_4$. Calculated %: N 13.92.

4. Conversion of 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane (II) to 2-(3'-ketocyclopentyl)-2-cyclohexylpropane (VI). a) Obtaining 4-(1'-methyl-1'-cyclohexylethyl)-adipic acid (V). To 105 g of 50% HNO_3 at 90° there were added 0.05 g of NH_4VO_3 and a few drops of (II). After rapid evolution of nitrogen oxides had begun, the mixture was cooled and 56 g of (II) was added stepwise at 40-50° with cooling and good stirring. After adding all the (II), the mixture was stirred for 1 additional hour at 60°, heated to 90°, air-blown to remove nitrogen oxides, and cooled to 0°. The separated oil was dissolved in benzene, washed with water, and stirred for 2 hours with 400 ml of 5% KOH solution. Upon acidification of the water layer the crude acid (V) separated as a thick brown oil, yield 54 g (80%).

To obtain the dimethyl ester, 35 g of methanol containing 7% hydrogen chloride was added to 30 g of (V) and the solution was left for 2 days at room temperature, after which it was washed with 10% sodium carbonate solution, washed with water, and extracted with ether. The ether extract was washed with salt solution and dried with anhydrous sodium sulfate. After distilling off the solvent, the residue (23 g) was vacuum distilled. There was obtained 17 g (52%) of the dimethyl ester of the acid (V), b. p. 175-190° (5 mm). A narrower fraction, containing 97% ester, was taken for analysis.

B. p. 174° (2 mm), d^{20}_4 1.0427, $n^{20}D$ 1.4820, MR_D 81.47; calc. 81.81.

Found %: C 68.30, 68.34; H 10.10, 10.11. $C_{17}H_{30}O_4$. Calculated %: C 68.41; H 10.13.

To obtain the pure acid (V), 19 g of its dimethyl ester and 180 ml of 15% KOH in alcohol-water were boiled for 3 hours in a water bath, after which the alcohol was distilled off, the residue was acidified with concentrated hydrochloric acid, and the separated oil was extracted with benzene, washed with salt solution, and dried with calcium chloride. The oil obtained (after distilling off the benzene) crystallized upon standing; m. p. 125-126° (after repeated washing with petroleum ether), acid content 98%.

Found %: C 66.96, 66.57; H 9.86, 9.92. $C_{15}H_{26}O_4$. Calculated %: C 66.63; H 9.69.

b) Obtaining 2-(3'-ketocyclopentyl)-2-cyclohexylpropane (VI). Upon heating 47 g of the crude acid (V) at 169-203° (5 mm), there was distilled off 24 g (67%) of a ketone fraction which was extracted with ether, washed with 5% KOH solution and with water, dried with calcium chloride, and (after distilling off the ether) vacuum distilled. The fraction with b. p. 139-141° (5 mm) [yield 50% calculated on (V)] was stirred 10 hours with excess 33% $NaHSO_3$ solution; the resulting bisulfite compound, after thorough washing with ether, was decomposed by sodium carbonate solution with simultaneous live-steam distillation of the liberated ketone. After vacuum distillation, (VI) was obtained with ketone content approximately 100% (determined by oxime formation).

B. p. 133° (2 mm), d^{20}_4 0.9862, $n^{20}D$ 1.5020, MR_D 62.34; calc. 62.46.

Found %: C 80.75, 80.95; H 11.21, 11.12. $C_{14}H_{24}O$. Calculated %: C 80.70; H 11.51.

Semicarbazone, shiny plates, m. p. 180° (from alcohol).

Found %: N 15.99, 16.09. $C_{15}H_{27}ON_3$. Calculated %: N 15.83.

2,4-Dinitrophenylhydrazone, orange plates, m. p. 101° (from methanol-chloroform, 3:1 by volume), λ_{max} (in CH_3OH) 365 mμ (log ε 4.37).

Found %: N 14.66, 14.55. $C_{20}H_{28}O_4N_4$. Calculated %: N 14.42.

c) Pyrolysis of 4-(1'-methyl-1'-cyclohexylethyl)-adipic acid (V). Upon heating 54 g of crude (V) with 6 g of $Ba(OH)_2$ at 235-350°, there was driven off 20 g of an oil and 5 g of water. The residue in the flask was a charred mass, from which no acidic products could be isolated. The principal fraction obtained upon distillation of the oil did not contain oxygen and had b. p. 150° (755 mm), d^{20}_4 0.8336, $n^{20}D$ 1.4598. This mixture of hydrocarbons was separated chromatographically on silica gel in a 10 mm x 1 m column with subsequent elution by hexane; a fraction was separated successfully which apparently consisted mainly of hexahydrocumene.

B. p. 148-149° (755 mm), d^{20}_4 0.8059, $n^{20}D$ 1.4392. Literature data [17]: b. p. 148° (760 mm), d^{20}_4 0.8023, $n^{20}D$ 1.4409.

Found %: C 85.83, 85.93; H 13.96, 13.97. C_9H_{18}. Calculated %: C 85.62; H 14.38.

The other hydrocarbon fractions obtained by chromatographic separation were discolored when shaken with concentrated H_2SO_4, and apparently contained tetrahydrocumenes and a small quantity of cumene, the latter having a strong characteristic odor.

5. Ring enlargement. Obtaining 2-(4'-ketocycloheptyl)-2-cyclohexylpropane (VII). To a solution of 85 g of (IV) in 250 ml of alcohol and 100 ml of ether, there was added 45 g of N-nitroso-N-methyl-p-toluenesulfamide (prepared with 73% yield according to a method described earlier [13]), and the mixture was stirred in such a manner that the undissolved N-nitroso-N-methyl-p-toluenesulfamide was only grazed lightly by the stirrer. To the reaction mixture (cooled to 5°) there was added very slowly a solution of 5 g KOH in 17 ml of

50% alcohol (temperature during addition of caustic 10-20°). The mixture was stirred 1 additional hour at room temperature and then acidified with 2N HCl. After distilling off the solvent, the reaction mixture was stirred vigorously for 6 hours with 100 ml of 33% $NaHSO_3$; the resulting bisulfite compound, after thorough washing with ether, was decomposed by sodium carbonate solution with simultaneous live-steam distillation of the liberated (VII). The yield of (VII) was 16.2 g (43%) with ketone content 99.6% (determined by oxime formation), m. p. 68-69° (from alcohol-water), small colorless plates; mixed sample with (IV) melted at 78°.

Found %: C 81.44, 81.15; H 11.95, 12.20. $C_{16}H_{28}O$. Calculated %: C 81.29; H 11.93.

Oxime, shiny square plates, m. p. 147-148° (from alcohol).

Found %: N 5.93, 5.77. $C_{16}H_{29}ON$. Calculated %: N 5.57.

Semicarbazone, colorless plates, m. p. 177° (from alcohol).

Found %: N 14.06, 14.29. $C_{17}H_{31}ON_3$. Calculated %: N 14.32.

2,4-Dinitrophenylhydrazone, small yellow crystals, m. p. 78-79° (from mixture of alcohol and ethyl acetate); λ_{max} (in CH_3OH) 366 mμ (log ε 4.38).

Found %: N 13.67, 13.70. $C_{22}H_{32}O_4N_4$. Calculated %: N 13.45.

From the filtrate, after removal of the bisulfite compound there was separated a crystalline substance with m. p. 74-75° (from water), identified as N-methyl-p-toluenesulfamide (mixed sample with known preparation of this compound did not give any depression of melting point), which probably was formed by denitrosation of the N-nitroso-N-methyl-p-toluenesulfamide under the action of caustic. Besides the N-methyl-p-toluenesulfamide, the filtrate probably contained also ethyl p-toluenesulfonate and compounds of high carbonyl number which, however, have not been studied in greater detail.

6. Conversion of the cycloheptanone (VII) to the cyclohexanone (IV). The ketone (VII) was oxidized with 50% HNO_3 as described for (IV). The acid thus formed (VIII) was converted to the dimethyl ester for purification.

B. p. 176-179° (3 mm), d^{20}_4 1.0350, $n^{20}D$ 1.4790, MR_D 86.0; calc. 86.43.

Found %: C 69.01, 69.29; H 10.40, 10.20. $C_{18}H_{32}O_4$. Calculated %: C 69.19; H 10.32.

The free acid (an oil) was separated by saponifying the dimethyl ester with KOH in water-alcohol; upon heating the acid under vacuum it was converted to the ketone (IV), identical with the ketone obtained by oxidation of (II).

SUMMARY

1. With the aim of synthesizing perfumes from 2-(p-hydroxyphenyl)-2-phenylpropane, which is available in large quantities, it was converted by hydrogenation to 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane, which was then oxidized to 2-(4'-ketocyclohexyl)-2-cyclohexylpropane. It was established that 2-(4'-hydroxycyclohexyl)-2-cyclohexylpropane and its acetate have only a faint and noncharacteristic odor, whereas 2-(4'-ketocyclohexyl)-2-cyclohexylpropane has a relatively strong distinctive odor.

2. To clarify the effect upon odor of the size of the ring carrying the ketone group, there was carried out the contraction of the six-membered ketonic ring in 2-(4'-ketocyclohexyl)-2-cyclohexylpropane to a five-membered ring and its enlargement to a seven-membered ring. It was shown that contraction of the ketonic ring leads to a marked intensification of odor, while enlargement of the ring is accompanied by weakening of odor.

LITERATURE CITED

1. V. M. Rodionov, V. N. Belov, and É. A. Simanovskaya, Trudy Vsesoyuz. Nauch.-Issledovatel. Inst. Sintet. i Nat. Dushistykh Veshchestv. 1, 38 (1952).
2. I. R. Byers, The Am. Perfumer and Essential Oil Review (1947), p. 483.
3. FRG Patent 834,593; Chem. Abs. 47, 5446 (1953).

4. FRG Patent 903,258, 903,259; Chem. Zentr. (1954), p. 5870.
5. GDR Patent 5051; Referat. Zhur. Khim. (1956), 11049.
6. GDR Patent 8201; Referat. Zhur. Khim. (1956), 11050.
7. V. N. Belov and L. A. Kheifits, Zhur. Obshch. Khim. 27, 960 (1957).*
8. L. A. Kheifits, É. A. Simanovskaya, V. N. Belov, P. V. Ivanov, E. S. Shapiro, and M. Ya. Braines, Masloboinozhirovaya Prom. 6, 35 (1957).
9. L. A. Kheifits, É. A. Simanovskaya, and V. N. Belov, Khim. Nauka i Prom. 3, 284 (1958).
10. L. A. Kheifits, G. I. Moldovanskaya, V. N. Belov, and L. N. Nikolenko, Khim. Nauka i Prom. 2, 658 (1957).
11. Synthesis of Organic Compounds, Collection I [in Russian] (1949), p. 15.
12. Synthesis of Organic Compounds, Collection I [in Russian] (1949), p. 518.
13. T. J. de Boer and H. J. Backer, Rec. trav. Chim. 73, 229 (1954).
14. T. J. de Boer and H. J. Backer, Rec. trav. Chim. 73, 589 (1954).
15. A. Socha and Z. Eckstein, Roczn. Chem. 32, 647 (1958).
16. I. S. Kizber, V. I. Isagulyants, and E. K. Smolyaninova, Syntheses of Perfumes [in Russian] (Pishchepromizdat, 1939), p. 256.
17. Beilst. V, 41.

* Original Russian pagination. See C. B. translation.

INVESTIGATION OF PYRAZOLES

VII. DEHYDROGENATION OF PHENYLPYRAZOLINES WITH FUNCTIONAL GROUPS ON THE BENZENE RING

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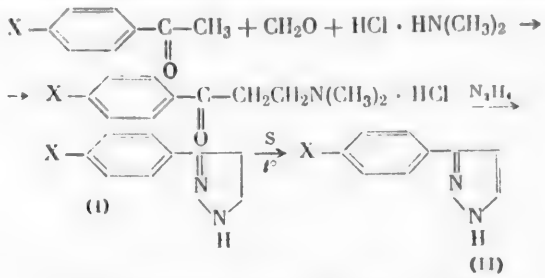
Original article submitted March 27, 1959

3-Phenylpyrazoles have a general soothing action on the central nervous system [1]; therefore we undertook a wider investigation of 3-arylpyrazoles, particularly compounds with functional groups on the benzene ring. The synthesis of a number of these compounds was reported recently on the basis of β-chlorovinyl ketones [2]; however, this method is not suitable for synthesizing compounds with substituents in the 4- and 5-positions of the pyrazole ring. Apart from this, we were interested in observing the behavior of various functional groups under conditions of dehydrogenation by sulfur, since a number of alkyl- and arylpyrazoles previously had been synthesized successfully by this method [3, 4].

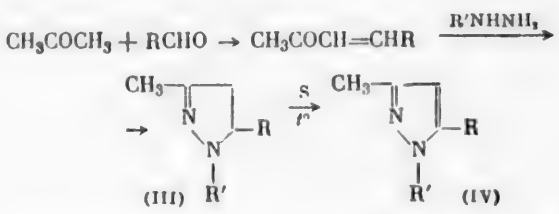
We carried out the dehydrogenation of 3-phenylpyrazolines (I) having a para-substituted alkyl, phenyl, chlorine, bromine, iodine, phenoxy , methoxy , or nitro group. It was shown that pyrazolines having an alkyl, phenyl, methoxy , or phenoxy group are dehydrogenated to the corresponding 3-arylpyrazoles (II) without affecting the functional group, although the yield of pyrazoles is somewhat lower than for analogous compounds without functional groups. The 3-arylpyrazolines (I) containing halogen, notwithstanding the evolution of hydrogen sulfide during the reaction, were completely resinified, so that the corresponding pyrazoles could not be found. The nitro group in the pyrazoline molecule also hindered the normal reaction course; severe carbonization occurred upon dehydrogenation. We made analogous observations for 1-aryl- and 5-arylpyrazolines. If the benzene ring of the pyrazoline carried a carboxy or sulfo group, then in general no evolution of hydrogen sulfide was observed and pyrazole formation did not occur even upon increasing the temperature to 250-300°. With a hydroxy or dimethylamino group, the dehydrogenation proceeded smoothly. All of our attempts to moderate the conditions of dehydrogenation were unsuccessful, including the use of a solution of sulfur in boiling xylene or the use of solid sodium thiosulfate. Conducting the usual reaction in a stream of sulfur dioxide likewise did not lead to any improvement of yields.

To synthesize the initial functionally substituted 3-arylpyrazolines (I) we used the Mannich reaction and subsequent treatment of the resulting β-dimethylaminopropiophenones with hydrazine hydrate [5, 6].



X = C_6H_5 (a), iso-C_3H_7 (b), CH_3O (c), C_6H_5O (d), Cl (e), Br (f), I (g), NO (h).

We synthesized 3,5-disubstituted pyrazolines (III) by the common method of interaction of the corresponding hydrazine with an unsaturated ketone. Dehydrogenation to the pyrazoles (IV) was carried out according to the usual method.



R = p-$(CH_3)_2NC_6H_4$, R′ = C_6H_5 (a); R = o-HOC_6H_4, R′ = H (b);
R = C_6H_5, R′ = p-$HOOCC_6H_4$ (c);
R = C_6H_5, R′ = p-$NaSO_3C_6H_4$ (d).

EXPERIMENTAL

3(5)-p-Ethylphenylpyrazole (IIa). A mixture of 28 g 3-p-ethylphenylpyrazoline (Ia) [5] and 5.2 g sulfur was heated in a Claisen flask at 180° for about 30 minutes. After hydrogen sulfide evolution had ceased, heating was continued for 20 minutes more to complete the reaction; the mixture was then vacuum distilled. The pyrazole was obtained as a viscous oil. Yield 20 g (71.5%), b. p. 188-190° at 10 mm.

Picrate, m. p. 195° (from alcohol).

Found %: N 17.57, 17.65. $C_{11}H_{12}N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 17.45.

1-Carbamido-3 (5)-p-ethylphenylpyrazole. To a solution of 5 g pyrazole (IIa) in 10 ml acetic acid, there was added 1.7 g potassium cyanate, and the mixture was heated to 90° for 15 minutes. Upon cooling the solution the amide crystallized. Yield 4.5 g (69%), m. p. 148° (from alcohol).

Found %: N 19.62, 19.68. $C_{12}H_{13}ON_3$. Calculated %: N 19.52.

3(5)-p-Isopropylphenylpyrazole (IIb). Obtained from 20 g 3-p-isopropylphenylpyrazoline (Ib) [6] as a viscous oil [method analogous to that used for 3(5)-p-ethylphenylpyrazole]. Yield 17 g (85%), b. p. 163° at 11 mm.

Picrate, m. p. 129° (from alcohol).

Found %: C 52.37, 52.54; H 4.30, 4.25. $C_{12}H_{14}N_2 \cdot C_6H_3O_7N_3$. Calculated %: C 52.14; H 4.15.

3(5)-p-Methoxyphenylpyrazole (IIc). Obtained from 15 g 3-p-methoxyphenylpyrazoline (Ic) [6] by method analogous to the foregoing. Yield 11.2 g (75%), m. p. 126° (from benzene).

Found %: C 69.27, 69.11; H 5.95, 5.93; N 15.97, 15.78. $C_{10}H_{10}ON_2$. Calculated %: C 68.94; H 5.79; N 16.02.

Hydrochloride of β-dimethylamino-p-phenoxypropiophenone. A mixture of 55 g p-phenoxyacetophenone (m. p. 42-44°) [7], 28 g dimethylamine hydrochloride, and 7.5 g paraform in 50 ml dioxane was refluxed for 1 hour, and the unreacted ketone was extracted by ether. The remaining solution was made alkaline with 40% sodium hydroxide solution, and the oil was extracted by ether. The ether extract was water washed and dried with fused sodium hydroxide. The solution was concentrated under vacuum and the resulting substance was dissolved in absolute ether. A stream of dry hydrogen chloride was passed through the dry ether solution, and the precipitated white mass was vacuum-dried over phosphorus pentoxide. Yield 60.5 g (80%), m. p. 133-135°.

Found %: N 4.01, 4.00. $C_{18}H_{22}O_2NCl$. Calculated %: N 4.38.

3-p-Phenoxyphenylpyrazoline (Id). To 40 ml of hydrazine hydrate, 20 ml 40% sodium hydroxide, and 100 ml methanol, there was added slowly with stirring at 40-42°, a solution of 50 g hydrochloride of β-dimethylamino-p-phenoxypropiophenone in 100 ml methanol, after which the reaction mixture was boiled for 0.5 hour. The precipitated white crystalline mass was water washed, filtered-off and pressed, and then heated with benzene above 100° to remove water. Yield 33 g (89%), m. p. 56-57°.

Picrolonate, m. p. 209° (from alcohol).

Found %: N 16.84, 16.67. $C_{15}H_{14}ON_2 \cdot C_{10}H_8O_5N_4$. Calculated %: N 16.74.

3(5)-p-Phenoxyphenylpyrazole (IId).* Obtained as a very viscous oil by dehydrogenation of 52 g 3-p-phenoxyphenylpyrazoline (Id) by a method analogous to that described previously. Yield 22.4 g (42%), b. p. 256° at 11 mm.

Picrate, m. p. 127-128° (from alcohol).

Found %: N 15.16, 15.12. $C_{15}H_{12}ON_2 \cdot C_6H_3O_7N_3$. Calculated %: N 15.06.

1-Carbamido-3-p-phenoxyphenylpyrazole, m. p. 133° (from alcohol).

Found %: C 69.07, 69.26; H 4.73, 4.80; N 15.04, 15.19. $C_{16}H_{13}O_2N_3$. Calculated %: C 68.78; H 4.73; N 15.09.

Hydrochloride of β-dimethylamino-p-iodopropiophenone. A mixture of 21 g p-iodoacetophenone (m. p. 83-84° [8]), 8 g dimethylamine hydrochloride, 3.2 g paraform, 25 ml alcohol, 20 ml dioxane and 0.2 ml concentrated hydrochloric acid was heated to boiling for 2.5 hours. After cooling, the salt of the β-dimethylaminoketone precipitated as white crystals. They were separated by vacuum filtration, washed with acetone, and recrystallized from 50% alcohol. Yield 19 g (65.5%), m. p. 201°.

Found %: C 38.97, 39.10; H 4.53, 4.56. $C_{12}H_{17}ONClI$. Calculated %: C 38.88; H 4.45.

3-p-Iodophenylpyrazoline (Ig). Obtained from 12 g hydrochloride of β-dimethylamino-p-iodopropiophenone, method same as for 3-p-phenoxyphenylpyrazoline. Yield 9 g (93%), m. p. 135-138°.

N-nitroso derivative, m. p. 167° (from alcohol).

Found %: C 35.88, 35.91; H 2.59, 2.64; N 13.80, 13.81. $C_9H_8ON_3I$. Calculated %: C 35.88; H 2.68; N 13.96.

Hydrochloride of β-dimethylamino-p-bromopropiophenone. Obtained from 90 g p-bromoacetophenone (m. p. 49° [9]), similar to experiment with p-iodoacetophenone. Yield 75 g (58%), m. p. 192° (from 50% alcohol). Literature data: m. p. 196° [10].

Found %: C 45.22, 45.12; H 5.35, 5.55. $C_{12}H_{17}ONClBr$. Calculated %: C 45.12; H 5.52.

3-p-Bromophenylpyrazoline (If). Obtained the same as p-iodophenylpyrazoline, from 50 g salt of the Mannich base, yield 85.5%, m. p. 130-133°. N-nitroso derivative, m. p. 158-159° (from alcohol).

Found %: C 42.58, 42.39; H 3.37, 3.19; N 16.34, 16.18. $C_9H_8ON_3Br$. Calculated %: C 42.50; H 3.17; N 16.54.

Hydrochloride of β-dimethylamino-p-chloropropiophenone. Obtained by the method described previously, from 75 g p-chloroacetophenone (b. p. 124-126° at 24 mm, m. p. 20-21° [9]), yield 61%, m. p. 170° (from 50% alcohol) [11].

3-p-Chlorophenylpyrazoline (Ie). Obtained from 50 g hydrochloride of β-dimethylamino-p-chloropropiophenone by the usual method, yield 83%, m. p. 89-92°.

N-nitroso derivative, m. p. 155° (from alcohol).

Found %: N 20.12, 19.96. $C_9H_8ON_3Cl$. Calculated %: N 20.04.

3-p-Nitrophenylpyrazoline (Ih). Obtained by the usual method by the action of hydrazine hydrate on the hydrochloride of β-dimethylamino-p-nitropropiophenone (m. p. 171° [12]), yield 64%, m. p. 156-157° [12].

* Student O. P. Shkurko took part in the synthesis of the 3(5)-p-phenoxyphenylpyrazole.

3-Methyl-5-p-dimethylaminophenyl-1-phenylpyrazoline (IIIa). To a solution of 10 g p-dimethylaminobenzalacetone (m. p. 132° [13]) in 150 ml acetic acid there was added 5.5 g phenylhydrazine. After 12 hours, 300 ml of water was added. The precipitate was recrystallized from ethyl acetate. Yield 12 g (75%), m. p. 166° [14].

3-Methyl-5-p-dimethylaminophenyl-1-phenylpyrazole (IVa). Obtained from 10.2 g pyrazoline (IIIa) by the method described previously. Yield 6.8 g (68%), m. p. 143-144° (from alcohol).

Found %: C 77.61, 77.52; H 6.95, 6.81; N 15.22, 15.43. $C_{18}H_{19}N_3$. Calculated %: C 77.94; H 6.92; N 15.14.

3-Methyl-5-(o-hydroxyphenyl)-pyrazoline (IIIb). A mixture of 50 g salicylalacetone (m. p. 137-139° [15]) and 50 ml ethyl alcohol was refluxed until dissolved, after which there was added dropwise 18 ml hydrazine hydrate, to which 4 drops of acetic acid had been added previously. The mixture was refluxed for 5 hours; the crystals which precipitated upon cooling were water washed and vacuum-dried 1 hour. Yield 25 g (45.4%), m. p. 105-106°.

1-Thiocarbamide derivative, m. p. 225° (from alcohol).

Found %: C 56.49, 56.52; H 5.68, 5.82. $C_{11}H_{13}ON_3S$. Calculated %: C 56.14; H 5.56.

3(5)-Methyl-5(3)-(o-hydroxyphenyl)-pyrazole (IVb). Obtained from 15 g pyrazoline (IIIb) by the method described previously, yield 53%, m. p. 130° (from 50% alcohol).

Found %: C 68.59, 68.73; H 5.73, 5.64; N 15.87, 16.01. $C_{10}H_{10}ON_2$. Calculated %: C 68.94; H 5.79; N 16.02.

3-Methyl-5-phenyl-1-(p-carboxyphenyl)-pyrazoline (IIIc). To a solution of 5.6 g hydrochloride of p-carboxyphenylhydrazine in 135 ml water there was added a solution of 4.4 g benzalacetone in 15 ml alcohol, and the mixture was heated to boiling for 30 minutes. Yellow crystals of the hydrazone precipitated, m. p. 193-194° [16]. For cyclization this hydrazone was boiled for 1 hour with 30 ml glacial acetic acid. After cooling, the pyrazoline precipitated as yellowish crystals. Yield 8.2 g (87.5%), m. p. 249-250° [16].

3-Methyl-5-phenyl-1-(p-sulfophenyl)-pyrazoline (IIId). In a flask fitted with a reflux condenser there were placed 5.5 g phenylhydrazine-p-sulfonic acid, 4.4 g benzalacetone, and 25 ml 80% acetic acid. The reaction mixture was refluxed for 5 hours; after cooling, it was made alkaline with 10% sodium hydroxide solution and then 20 ml saturated sodium chloride solution was added with further cooling. The precipitated sodium salt was recrystallized from alcohol. Yield 5.8 g (60%) [17].

Found %: N 8.30, 8.46. $C_{16}H_{15}O_3N_2SNa$. Calculated %: N 8.28.

SUMMARY

1-, 3-, or 5-arylpyrazolines which have an alkoxy , phenoxy , dimethylamino , or hydroxy group substituted on the benzene ring are dehydrogenated by sulfur to the corresponding pyrazoles. Pyrazolines with a halogen, sulfo , carboxy , or nitro group on the benzene ring are resinified upon heating with sulfur, apparently at the expense of reaction of the functional group.

LITERATURE CITED

1. G. A. Pershin, N. A. Novitskaya, A. N. Kost, and I. I. Grandberg, Doklady Akad. Nauk SSSR 123, 200 (1958).*
2. N. K. Kochetkov, E. D. Khomutova, O. B. Mikhailova, and A. N. Nesmeyanov, Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk (1957), p. 1181.*
3. I. I. Grandberg and A. N. Kost, Zhur. Obshch. Khim. 28, 3071 (1958).*
4. I. I. Grandberg and A. N. Kost, Zhur. Obshch. Khim. 29, 658 (1959).*

* Original Russian pagination. See C. B. translation.

5. V. V. Ershov, A. N. Kost, and A. P. Terent'ev, Zhur. Obshch. Khim. 27, 260 (1957).*
6. A. N. Kost and V. V. Ershov, Vestnik Moskovsk. Gosudarst. Univ. 12, 115 (1955).
7. F. Kipper, Ber. 38, 2491 (1905).
8. R. Strassburg, R. Gregg, and C. Walling, J. Am. Chem. Soc. 69, 2141 (1947).
9. Synthesis of Organic Compounds, Collection I [in Russian] (1949), p. 104.
10. E. Knott, J. Chem. Soc. (1947), p. 1193.
11. I. Dhont and I. Wibaut, Rev. trav. chim. 63, 81 (1944).
12. V. V. Ershov, Dissertation (MGU, 1958).
13. L. Raiford and M. Cooper, J. Org. Chem. 3, 13 (1938).
14. L. Raiford and E. Mill, J. Am. Chem. Soc. 56, 174 (1934).
15. T. Thomson, J. Chem. Soc. Ind. 65, 121 (1946).
16. S. Veibel, Acta Chim. Scand. 1, 54 (1947).
17. British Patent 698,253 (1953); Chem. Abs. 48, 6136 (1954).

* Original Russian pagination. See C. B. translation.

A NEW CONVERSION IN THE CHROMONE SERIES

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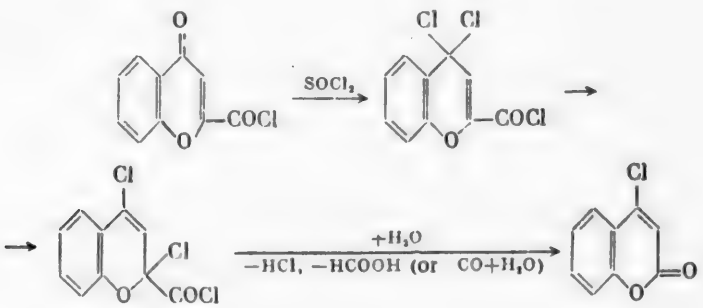
Original article submitted March 26, 1959

In communication [1] we reported that, depending on the conditions, chromone-2-carboxylic acid reacts with excess thionyl chloride to give mainly either the acid chloride or (after water treatment) a chlorine-containing substance of unknown structure with m. p. 93-94°, which was also obtained from the acid chloride by treating the latter with thionyl chloride.

In the present work we established that this chlorine-containing compound is identical with 4-chlorocoumarin, which was prepared previously in low yields by treating 4-hydroxycoumarin with phosphorus pentachloride [2] or phosphorus oxychloride [3]. In the papers cited, the 4-chlorocoumarin was not isolated in a pure state. According to data in [2], this substance melts at 91-92° and according to [3], its m. p. is 89-91°. We established that thoroughly purified 4-chlorocoumarin, synthesized from chromone-2-carboxylic acid and from 4-hydroxycoumarin by the method in [3], has m. p. 95-95.5°. Both samples of 4-chlorocoumarin reacted with aniline and piperidine to give 4-anilino- and 4-piperidinocoumarins, which were described in [2]. The identity of our chlorine-containing compound with 4-chlorocoumarin was also confirmed by a series of other reactions (see Experimental).

It may be assumed that the γ-benzopyrone system is converted into the α-benzopyrone system by the following scheme.



Further investigations are being carried out to elucidate the limits of applicability of this interesting conversion and to determine the reaction mechanism more accurately.

EXPERIMENTAL

4-Chlorocoumarin. a) The preparation obtained previously [1] in 87% yield was purified by distillation (b. p. 147° at 6 mm) and recrystallized from alcohol. The colorless needles had m. p. 95-95.5°.

Found %: C 59.55; H 2.79; Cl 19.69. $C_9H_5O_2Cl$. Calculated %: C 59.86; H 2.79; Cl 19.62.

b) 4-Hydroxycoumarin (1.25 g) and 0.75 g of $POCl_3$ were heated on a bath at 110-115° for 2 hours. The mixture was decomposed with ice and the red precipitate collected by filtration, dried and distilled (the b. p. was about 120° at 2 mm). Recrystallization from alcohol (charcoal) yielded 0.5 g of substance with m. p. 95-95.5°. A mixed melting point with a sample prepared from chromone-2-carboxylic acid was not depressed.

Reduction of 4-chlorocoumarin (from chromone-2-carboxylic acid). a) In accordance with the data in [2], reduction of the substance with zinc dust in a mixture of aqueous alcohol and acetic acid gave coumarin; the yield was 82% and the m. p. 67-68° (from a mixture of ligroin and benzene).

b) 4-Chlorocoumarin (1.08 g) was hydrogenated in the presence of 0.2 g of 10% $Pd/BaSO_4$ in 70 ml of alcohol until 1 mole of H_2 had been absorbed. We isolated 0.88 g of coumarin.

4-Anilinocoumarin. This compound was prepared by the procedure in [2]: aniline was heated (180°, 20 minutes) with 4-hydroxycoumarin or with 4-chlorocoumarin, synthesized from chromone-2-carboxylic acid and from 4-hydroxycoumarin. The substance had m. p. 268-269° (from alcohol). According to data in [2]: m. p. 259-260°.

4-Piperidinocoumarin. This compound was prepared from the two preparations of 4-chlorocoumarin described above by heating them with piperidine (105-110°, 20 minutes) [2]. The m. p. was 105-106° (from 50% alcohol). A mixture of the two samples of 4-piperidinocoumarin melted without depression. According to data in [2]: m. p. 104-105°.

4-Methoxycoumarin. a) A solution of 1.8 g of 4-chlorocoumarin (from chromone-2-carboxylic acid) in 60 ml of anhydrous methanol was mixed with a solution of sodium methylate (from 0.25 g of sodium and 10 ml of methanol). After 2 days (approximately 20°) the mixture was cooled to 0°. The crystalline precipitate (fine colorless needles) were collected by filtration and dried. The mother liquor yielded more of the substance. The total yield was 1.5 g (85%) and the m. p. was 124.5°. According to data in [4] (in which the substance was synthesized by methylation of 4-hydroxycoumarin) the m. p. is 125°.

SUMMARY

It was established that when chromone-2-carbonyl chloride reacts with thionyl chloride, 4-chlorocoumarin is formed as a result of conversion of the γ-benzopyrone system to the α-pyrone system.

LITERATURE CITED

1. V. A. Zagorevskii, D. A. Zykov, and L. P. Pronina, Zhur. Obshch. Khim. 29, 1026 (1959).*
2. R. Anschütz, Lieb. Ann. 367, 169 (1909).
3. D. Spalding, et al., J. Am. Chem. Soc. 72, 5338 (1950).
4. F. Arndt, et al., Ber. 84, 319 (1951).

* Original Russian pagination. See C. B. translation.

REACTION OF ETHOXYCHLOROQUINONES WITH AMINES

I. REACTIONS OF DIETHOXYDICHLORO-1,4-BENZOQUINONES

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According to the literature [1-3], 2,5-dimethoxy- and 2,5-diethoxy-1,4-benzoquinones react with ethyleneimine and other amines under relatively mild conditions to give 2,5-diaminobenzoquinone derivatives. In contrast to 2,5-dialkoxyquinones, 2,6-dialkoxybenzoquinones react with ethyleneimine and other amines with difficulty [1, 4, 5]. The introduction of halogen atoms into 2,5-dialkoxy and 2,6-dialkoxy derivatives of benzoquinones increases the reactivity of their alkoxy groups. Thus, Kerman [6-8] showed that the alkoxy groups in 2,5-dialkoxy-3,6-dichlorobenzoquinones are replaced by aliphatic amine and aniline residues in the cold to form 2,5-diamino-3,6-dichlorobenzoquinone derivatives. The reaction of 2,6-dialkoxy-3,5-dichlorobenzoquinone with the same amines required slight heating; this gave derivatives of 2,5-diamino-3-alkoxy-6-chlorobenzoquinone.

It is curious that up to now, as far as we know from the literature, no derivatives of 2,6-diaminobenzoquinone or of 2,6-diamino-3,5-dichlorobenzoquinone have been prepared (except for 2,6-diacetyl diaminobenzoquinone [9, 10] or of 2,3,5-trianilinobenzoquinone [11], which were synthesized by an indirect method). In this connection, it is interesting to note the recent observation of Marxer [4] who treated 2,6-dimethoxy-3,5-dibromoquinone with ethyleneimine in the cold and thus was the first to prepare 2,6-diethyleneimine-3,5-dibromoquinone.*

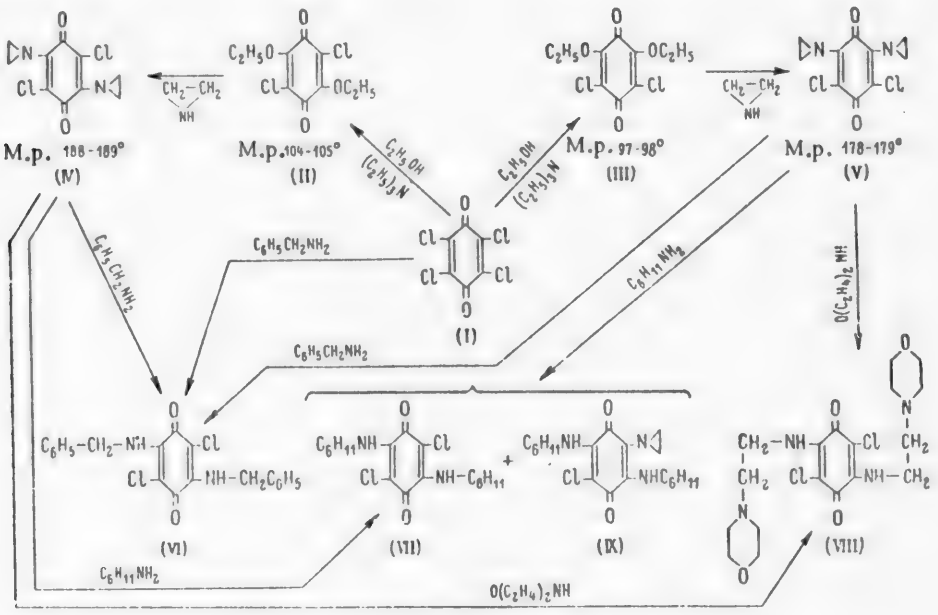
In the present work we established some new, noteworthy facts by studying the reactions of 2,5-diethoxy-3,6-dichlorobenzoquinone and 2,6-diethoxy-3,5-dichlorobenzoquinone with amines.

The 2,5-diethoxy-3,6-dichloro-1,4-benzoquinone (II) and 2,6-diethoxy-3,5-dichloro-1,4-benzoquinone (III) required for the investigation were prepared by heating an alcohol suspension of chloranil (I) in the presence of triethylamine with a molar ratio of chloranil to triethylamine of 1 : 2. We should note here that a molar ratio of the components of 1 : 0.25 gave only monoethoxytrichloroquinone, whose preparation and reactions will be described in the next communication. A chloranil to triethylamine ratio of 1 : 1 gave a mixture of all three ethoxychlorobenzoquinones.

2,5-Diethoxy-3,6-dichloroquinone reacted with ethyleneimine in an alcohol medium in the cold to give 2,5-diethyleneimino-3,6-dichloroquinone (IV), which is also formed by the reaction of chloranil with ethyleneimine [3]. Similarly, under the same conditions 2,6-diethoxy-3,5-dichloroquinone and ethyleneimine readily gave a good yield of 2,6-diethyleneimino-3,5-dichloroquinone (V) as lavender needles. At the same time, it was shown that the preparation of these diethyleneiminodichloroquinones did not require pure diethoxydichloroquinones and that mixtures of them could be used as starting materials. Treatment of an alcohol solution of such a mixture with ethyleneimine in the cold first gave a red-brown precipitate of 2,5-diethyleneimino-3,6-

* After the present article had been written, the report by Gauss [15] appeared and in this he gives data on the preparation of 2,6-bis(dimethylamino)-1,4-benzoquinone. In other respects, the contents of this paper agree with our observations.

dichloroquinone, which is difficultly soluble in alcohol, and then cooling the filtrate gave the relatively soluble 2,6-diethyleneimino-3,5-dichloroquinone.



As was reported previously [12, 13], reaction of 2,5-diethyleneiminobenzoquinones with various amines results in either the opening of the ethyleneimine ring or the replacement of the whole ethyleneimine group by the residue of the corresponding amine to form 2,5-diaminoquinone derivatives.

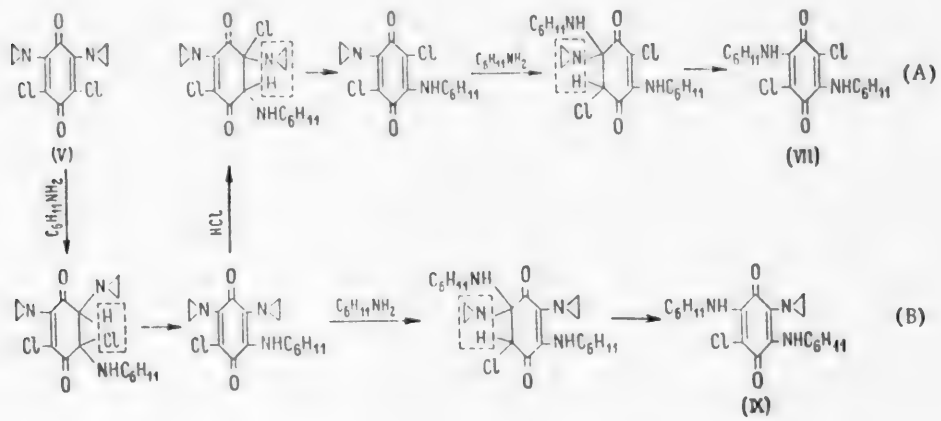
It seemed interesting to use this reaction for the preparation of derivatives of 2,6-diamino-3,5-dichloroquinone. However, on treating 2,6-diethyleneimino-3,5-dichlorobenzoquinone (V) with benzylamine, cyclohexylamine and morpholine, we encountered a new, interesting type of rearrangement. Instead of derivatives of 2,6-diamino-3,5-dichlorobenzoquinone, derivatives of 2,5-diamino-3,6-dichlorobenzoquinone were formed (VI, VII, and VIII), i.e., the same compounds as were obtained from 2,5-diethyleneimino-3,6-dichlorobenzoquinone (IV) or chloranil (I) and the given amines.

Thus, in this case there is an interchange of positions between the amine residue and the chlorine atom at the carbon atoms connected by double bonds. What is particularly interesting is that this rearrangement occurred even under the action of morpholine, which does not displace ethyleneimino groups from the molecules but merely opens the ethyleneimine ring.

The mechanism of this rearrangement may be represented by scheme A, which illustrates the reaction with cyclohexylamine. A series of successive additions at the double bond and eliminations of the elements of the amine and hydrogen chloride occur in this scheme. Obviously, if we accept such an explanation for the given rearrangement, which includes several stages, then we must assume that numerous side reactions are possible and as a result the yield of rearrangement product will be low as compared with the yield of the same product from 2,5-diethyleneimine-3,6-dichloroquinone (IV), as the table shows.

The reaction of 2,6-diethyleneimino-3,5-dichlorobenzoquinone (V) with cyclohexylamine illustrated by the scheme gave, in addition to the rearrangement product (VII), another substance with a blue-green color and m. p. 134-135°. According to the analysis results, this substance was apparently 2,5-dicyclohexylamino-3-ethyleneimino-6-chloro-1,4-benzoquinone (IX), i.e., a substance which could have been an intermediate product in the chain of conversions of 2,6-diethyleneimino-3,5-dichloroquinone (V) to 2,5-dicyclohexylamino-3,6-dichloroquinone (VII). However, by starting with pure triaminochloroquinone (IX), we could not prepare the diaminodichloroquinone (VII) using the same or similar conditions to those under which the latter was formed from quinone (V). We therefore consider that the formation of 2,5-dicyclohexylamino-3-ethyleneimino-6-chlorobenzoquinone (IX) occurs simultaneously with the formation of 2,5-dicyclohexylamino-3,6-dichloroquinone

(VII) according to scheme (B). Also, it is possible that in these cases the addition and displacement processes occur in the 1,4 and not the 1,2 position.



A comparison of the literature data given with the results we obtained shows that various dialkoxybenzoquinones react with amines with different facility to give various compounds, depending on the structure of the dialkoxyquinone and the nature of the amine used.

Results of Experiments on the Reaction of 2,5-Diethyleneimino-3,6- dichlorobenzoquinone (IV) and 2,6-Diethyleneimino-3,5-dichlorobenzoquinone (V) with Amines

Starting material		Solvent	Reaction time (in min)	Substance obtained	Yield (in %)	Melting point	Color of crystals
quinone	amine						
(IV)	Benzylamine	CH_3OH	5	(VI)	90	222—223°	Yellow-orange
(V)	Benzylamine	CH_3OH	35	(VI)	50		
(IV)	Cyclohexylamine	CH_3OH	13	(VII)	93	233—234	Pink
(V)	Cyclohexylamine	CH_3OH	120	(VII)	30		
(IV)	Morpholine	None	10	(VIII)	80	188—189	Light brown
(V)	Morpholine	None	10	(VIII)	32		
(V)	Morpholine	CH_3OH	75	(VIII)	45		

On the basis of a study of the reactions of dimethoxybenzoquinones with amines and ethyleneimine, Marxer [4] put forward the hypothesis that the reactivity of these compounds depends on the distribution of the electron density at the carbon atoms connected to the methoxyl groups. In 2,6-dimethoxybenzoquinone, the positive charges at the carbon atoms connected to the methoxyl groups are a factor of two less than those of the corresponding atoms in 2,5-dimethoxybenzoquinone. In 2,6-dimethoxy-3,5-dibromobenzoquinone, the bromine atoms promote an increase in the positive charge at the carbon atoms bearing the methoxyl groups; as a result, replacement of the methoxyl groups by ethyleneimine residues becomes a possibility.

On the basis of our investigations, we consider that only amines of the ethyleneimine type, which have an "aromatic" character, may directly enter the 2,6-position in 2,6-dialkoxy-3,5-dihalobenzoquinones under the given conditions. Apparently, benzylamine, cyclohexylamine, and similar amines are not held by the weak positive charges at the position 2,6, and in attempts to prepare derivatives of 2,6-diamino-3,5-dichlorobenzoquinone, a rearrangement occurs which gives the more stable derivatives of 2,5-diamino-3,6-dichlorobenzoquinone.

EXPERIMENTAL

2,5-Diethoxy-3,6-dichloro-1,4-benzoquinone (II) and 2,6-diethoxy-3,5-dichloro-1,4-benzoquinone (III). A suspension of 1 g of finely ground chloranil in 15 ml of alcohol and 1.1 ml of triethylamine (molar ratio of chloranil to triethylamine 1 : 2) were heated on a boiling water bath for 20 minutes. After 10 minutes, all the chloranil dissolved and the solution became dark green. Evaporation of the solution in vacuum and extraction of the residue with ligroin yielded 0.9 g (83%) of a mixture of diethoxydichloroquinones with m. p. 70-80°. Fractional recrystallization of 1 g of the diethoxydichloroquinone mixture from ligroin gave two compounds: 2,5-diethoxy-3,6-dichloro-1,4-benzoquinone (II) in the form of garnet red plates with m. p. 104-105° (0.38 g, 38%) and 2,6-diethoxy-3,5-dichloro-1,4-benzoquinone (III) in the form of lustrous, yellow-orange leaves with m. p. 97-98° (0.4 g, 40%). Mixed melting points of these compounds with 2,5-diethoxy-3,6-dichloroquinone and with 2,6-diethoxy-3,5-dichloroquinone, respectively, prepared by Kehrmann's method [6-8], were not depressed.

2,5-Diethyleneimino-3,6-dichloro-1,4-benzoquinone (IV). Ethyleneimine (0.2 ml) was added dropwise to a cooled solution of 0.5 g of (II) in 25 ml of alcohol. The solution became dark cherry-red and a red-brown precipitate formed (0.45 g, 93%). After two recrystallizations from a mixture of methanol and chloroform (1 : 1), the red-brown needles had m. p. 188-189°. A mixed melting point of the compound obtained with 2,5-diethyleneimino-3,6-dichloroquinone [3] was not depressed.

2,6-Diethyleneimino-3,5-dichloro-1,4-benzoquinone (V). Ethyleneimine (0.2 ml) was added dropwise to a solution of 0.5 g of (III) in 25 ml of alcohol, cooled in ice water. The solution became dark cherry-red and a voluminous, flocculent lavender precipitate formed (0.4 g, 80%). Two recrystallizations from alcohol yielded lavender needles of 2,6-diethyleneimino-3,5-dichloroquinone with m. p. 178-179°. The substance was insoluble in water but dissolved readily in alcohol and other organic solvents.

Found %: C 46.12; H 3.36; N 10.80; Cl 27.64. $C_{10}H_8O_2N_2Cl_2$. Calculated %: C 46.36; H 3.12; N 10.81; Cl 27.37.

Preparation of 2,5-diethyleneimino-3,6-dichloro-1,4-benzoquinone (IV) and 2,6-diethyleneimino-3,5-dichloro-1,4-benzoquinone (V) from a mixture of diethoxydichlorobenzoquinones. Ethyleneimine (0.4 ml) was added dropwise to an ice-cooled aqueous solution of 1 g of the diethoxydichloroquinone mixture (m. p. 78-80°) in 50 ml of alcohol. The solution became dark cherry-red. After 2 minutes a dark red precipitate of 2,5-diethyleneimino-3,6-dichloro-1,4-benzoquinone (IV) began to form and this was rapidly collected by filtration. The yield was 0.43 g (87%). Cooling the filtrate in a refrigerator yielded a lavender precipitate of 2,6-diethyleneimino-3,5-dichloro-1,4-benzoquinone (V). The yield was 0.4 g (80%).

2,5-Dibenzylamino-3,6-dichloro-1,4-benzoquinone (VI). A suspension of 0.1 g of V in a mixture of 0.32 ml of benzylamine and 0.25 ml of methanol was boiled for 35 minutes. Cooling the solution yielded a yellow-orange precipitate. The weight was 0.07 g (50%). After two recrystallizations from a mixture of methanol and chloroform (1 : 1), the substance had m. p. 222-223°. A mixed melting point of the compound with 2,5-dibenzylamino-3,6-dichlorobenzoquinone prepared from chloranil and benzylamine [14] or from 2,5-diethyleneimino-3,6-dichlorobenzoquinone and benzylamine [13] was not depressed.

2,5-Dicyclohexylamino-3,6-dichloro-1,4-benzoquinone (VII) and 2,5-dicyclohexylamino-3-ethyleneimino-6-chloro-1,4-benzoquinone (IX). A suspension of 0.1 g of (V) in a mixture of 0.32 ml of cyclohexylamine and 2.5 ml of methanol was boiled for 2 hours. After approximately 10 minutes the first lustrous pink crystals appeared and the solution became greenish-blue. Filtration of the hot solution yielded 0.04 g (30%) of a pink precipitate with m. p. 233-234°. A mixed melting point of the compound isolated with 2,5-dicyclohexylamino-3,6-dichlorobenzoquinone prepared by reacting 2,5-diethyleneimino-3,6-dichlorobenzoquinone with cyclohexylamine [13] was not depressed. Cooling of the dark filtrate yielded the greenish-blue crystals of 2,5-dicyclohexylamino-3-ethyleneimino-6-chloro-1,4-benzoquinone (IX). The yield was 0.05 g. After two recrystallizations from alcohol, the substance had m. p. 134-135°. The substance was insoluble in water but soluble in organic solvents.

Found %: C 63.49; H 7.49; N 11.07; Cl 9.57. $C_{20}H_{28}O_2N_3Cl$. Calculated %: C 63.57; H 7.48; N 11.13; Cl 9.40.

2,5-Di-(β-morpholinylethylamino)-3,6-dichloro-1,4-benzoquinone (VIII). a) A suspension of 0.1 g of (V) in 0.75 ml of morpholine was heated to boiling for 10 minutes. The precipitate dissolved to give a dirty pink solution. Dilution of the solution with methanol yielded a light brown precipitate. The weight was 0.05 g (32%). Two recrystallizations from a mixture of methanol and chloroform (1:1) yielded golden-light brown plates with m. p. 188-189°. A mixed melting point of the compound with 2,5-di-(β-morpholinylethylamino)-3,6-dichlorobenzoquinone prepared from 2,5-diethyleneimino-3,6-dichloroquinone and morpholine [12] was not depressed.

b) A suspension of 0.1 g of (V) in a mixture of 0.26 ml of morpholine and 2 ml of methanol was boiled for 75 minutes. The solution was cooled to give 2,5-di-(β-morpholinylethylamino)-3,6-dichloro-1,4-benzoquinone (VIII). The yield was 0.07 g (45%).

SUMMARY

1. It was shown that reaction of chloranil with alcohol in the presence of triethylamine, with a 1:2 molar ratio of chloranil to triethylamine, gave a mixture of 2,5-diethoxy-3,6-dichloro-1,4-benzoquinone and 2,6-diethoxy-3,5-dichloro-1,4-benzoquinone.

2. 2,5-Diethoxy-3,6-dichlorobenzoquinone and 2,6-diethoxy-3,5-dichlorobenzoquinone reacted with ethyleneimine to give 2,5-diethyleneimino-3,6-dichloro-1,4-benzoquinone and 2,6-diethyleneimino-3,5-dichloro-1,4-benzoquinone.

3. It was established that during the reaction of 2,6-diethyleneimino-3,5-dichlorobenzoquinone with amines there is a rearrangement which results in the formation of derivatives of 2,5-diaminobenzoquinone that are identical with those obtained previously by reacting 2,5-diethyleneimino-3,6-dichlorobenzoquinone with the same amines.

LITERATURE CITED

1. W. K. Anslow and H. Raistrick, J. Chem. Soc. (1939), p. 1446.
2. I. S. Ioffe and A. F. Sukhina, Zhur. Obshch. Khim. 24, 705 (1954).*
3. S. Petersen, W. Gauss, and E. Urbschat, Angew. Chem. 67, 217 (1955).
4. A. Marxer, Helv. Chim. Acta 40, 502 (1957).
5. H. O. Huisman, Rec. trav. chim. 69, 1133 (1950).
6. F. Kehrmann, J. Prakt. Ch. (2), 39, 318 (1889).
7. F. Kehrmann, J. Prakt. Ch. (2), 40, 367 (1889).
8. F. Kehrmann, J. Prakt. Ch. (2), 43, 260 (1891).
9. Bamberger, Ber. 16, 2402 (1883).
10. Nietzki and Preusser, Ber. 20, 797 (1887).
11. W. Gundel and R. Pummerer, Lieb. Ann. 529, 11 (1937).
12. A. N. Makarova and A. Ya. Berlin, Zhur. Obshch. Khim. 29, 666 (1959).*
13. A. N. Makarova and A. Ya. Berlin, Zhur. Obshch. Khim. 29, 3959 (1959).*
14. N. P. Buu-Hoï and R. Rover, Rec. trav. chim. 71, 1059 (1952).
15. W. Gauss, Ber. 91, 2216 (1958).

* Original Russian pagination. See C. B. translation.

ACYL DERIVATIVES OF BARBITURIC ACID

I. N-BENZOYLLUMINAL

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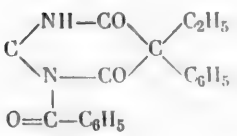
Barbituric acid derivatives find application as valuable medicinal preparations, generally with a hypnotic and narcotic action (veronal, luminal, barbamyl, hexenal, etc.). Acyl derivatives of barbiturates have been studied little [1, 2], especially those which contain carboxylic acid residues in the 1,3-positions, i.e., on one or two of the nitrogen atoms of the heterocycle.

According to patent data [3], diacylated barbiturates are good hypnotics and are less toxic than the corresponding barbiturates without acyl residues.

Henze and Spurlock [4] prepared some monoacyl derivatives of luminal and of these, N-propionyl- and N- α-bromodiethylacetylluminals deserve attention as, according to the data of the authors, they have quite strong antispasmodic properties.

In order to increase the anticonvulsive action of the compounds, we synthesized benzoyl derivatives of some barbiturates, in the first instance, luminal.


(I)

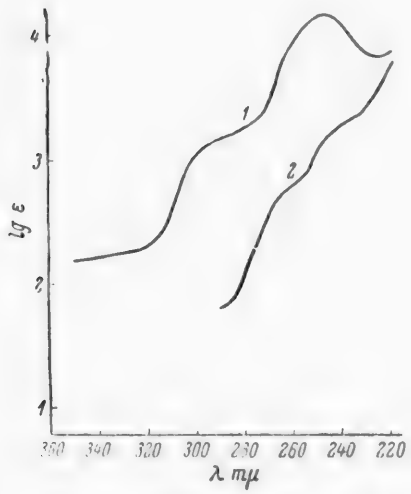
N-Benzoylluminal (I), which we called "benzonal," was prepared by two methods. The first of these consisted of treatment of the sodium or potassium salt of luminal with benzoyl chloride and the second, treatment of free luminal with benzoyl chloride in pyridine solution. In both cases the unreacted luminal was readily recovered and could be reused for the synthesis of benzonal without additional purification.

Benzonal formed a white, finely crystalline powder with a weak unusual odor. It had m. p. 134-135°. It was insoluble in water, but dissolved readily in hot alcohol, acetone, benzene, and chloroform. It crystallized from alcohol as small rhombic crystals. The absorption curve obtained with an SF-4 spectrophotometer differed substantially from that of luminal and may be used as a criterion of the preparation purity (see figure).

According to the pharmacological investigations of E. M. Dumenova, benzonal shows a strong antispasmodic action when administered intravenously as a 3% suspension in a 1-2% starch paste at a dose of 0.01 g/kg weight of the experimental animal (dogs, cats, and rabbits). With hypodermic and internal administration, spasms are eliminated and their appearance prevented by a dose of 0.06 g/kg (experiments on guinea pigs). It was less toxic than luminal, but much more active. It did not have a soporific action in therapeutic doses. According to the preliminary data of N. V. Shubin, benzonal has a considerable therapeutic effect in serious forms of epilepsy (observations on 20 patients), does not give the unpleasant side reactions characteristic of luminal, and is readily tolerated by patients during its prolonged use (more than 4 months).

EXPERIMENTAL

Preparation of benzoylluminal from the sodium salt of luminal. Into a three-necked flask fitted with a stirrer, reflux condenser with a calcium chloride tube, and a dropping funnel was placed 25.4 g of freshly prepared dry sodium salt of luminal, obtained by the action of sodium ethylate on luminal [5]. The contents of the flask were heated on an oil bath (140°) and 14 g (11.3 ml) of freshly distilled benzoyl chloride added dropwise. The bath temperature was raised to 180° and the reaction carried out for 6 hours with vigorous stirring. The bath was cooled to 75-80°, 100 ml of dry benzene added, and the mixture stirred for 15-20 minutes. The liquid was decanted, the residue treated 2-3 times with fresh 50 ml portions of benzene, and the combined benzene extracts left to stand for 10-12 hours. The precipitate was collected, dried at 60°, and recrystallized 2-3 times from alcohol. The yield of benzoylluminal with m. p. 134-135° was about 8.4 g (25%).



Ultraviolet absorption curves. 1) N-Benzoylluminal; 2) luminal.

Found %: C 67.81, 68.01; H 4.50, 4.76; N 8.25, 8.31. $C_{19}H_{16}O_4N_2$. Calculated %: C 67.85; H 4.79; N 8.33.

Preparation of benzoylluminal from luminal. A mixture of 23.2 g of luminal and 7.9 g of pyridine was heated to 100° on an oil bath, 14 g of freshly distilled benzoyl chloride added dropwise, and the stirrer started. The bath temperature was raised to 135° and the reaction continued for 6 hours. The mixture was cooled and washed 3-4 times with benzene (30-40 ml portions) by decantation to remove unreacted benzoyl chloride. The sirupy mass was transferred to a crystallizing dish and left in a vacuum desiccator for the removal of traces of benzene. The reaction mass was then washed repeatedly with cold water until the smell of pyridine disappeared and when it had solidified, it was collected and dried at 40°. Recrystallization from alcohol (3-4 times) gave 15-16 g (45-48%) of pure benzonal.

SUMMARY

Methods were developed for preparing N-benzoylluminal ("benzonal") from luminal and its sodium salt. By pharmacological tests and preliminary clinical trials it was established that benzonal has a strong antispasmodic action, is less toxic than luminal, and does not show a hypnotic effect in therapeutic doses.

LITERATURE CITED

1. Biltz and Witter, Chem. Zentr. (1921), III, 336.
2. Biltz and T. Köhler, Chem. Abs. 18, 1472 (1924).
3. German Patent 631,097; Chem. Abs. 31, 6136 (1936).
4. H. Henze and I. Spurlock, J. Am. Chem. Soc. 63, 3360 (1948).
5. R. Cematescu, Chem. Abs. 33, 4961 (1939).

SOME REACTIONS OF RICINOLEIC ACID AND ITS DERIVATIVES

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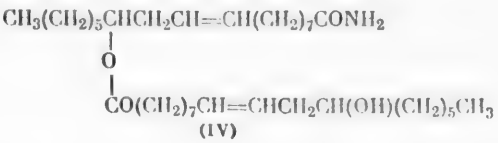
Ricinoleic acid and some of its salts and esters have antibacterial properties [1-3] and a certain antiviral activity [4-6] and also show a bacteriostatic action against leprosy [7] and tuberculosis [8] bacteria. Therefore, it seemed interesting to prepare some derivatives of ricinoleic acid that have not been investigated as yet so as to test their biological activity.

We obtained pure ricinoleic acid from castor oil. Treatment of the oil with a methanol solution of hydrogen chloride gave methyl ricinoleate and the action of acetic anhydride on the latter yielded the acetyl derivative, which was hydrolyzed with an alcohol solution of potassium hydroxide.

Ricinoleic acid derivatives could be prepared only under mild conditions in the absence of acidic agents. Thus, shaking methyl ricinoleate with a methanol solution of ammonia gave the amide of ricinoleic acid (I) and boiling ricinoleic ester with hydrazine hydrate in alcohol gave the hydrazide of ricinoleic acid (II). In most other cases in attempts to prepare ricinoleic acid derivatives, reaction occurred at the 12-hydroxy group. For example, in attempts to prepare the acid chloride of ricinoleic acid even under the mildest conditions (action of thionyl chloride at room temperature), we obtained the acid chloride of 12-chlorooleic acid, which lost hydrogen chloride during vacuum distillation and was converted into the acid chloride of octadeca-9,11-dienoic acid. The formation of the acid chloride of 12-chlorooleic acid was confirmed by the fact that treatment of ricinoleic acid with thionyl chloride in the cold and subsequent treatment with phenol yielded a halogenated ester, which lost hydrogen chloride during vacuum distillation and was converted into the phenyl ester of octadeca-9,11-dienoic acid (III). The hydroxyl was readily replaced by chlorine, even by the action of thionyl chloride on methyl ricinoleate.

In an attempt at the preparation of the nitrile of ricinoleic acid from its amide, ammonia was eliminated at the expense of the amide group of one molecule and the hydroxyl group of another with the formation of an ester, which apparently had structure (IV).



(IV)

The action of acetic anhydride on the amide of ricinoleic acid gave the nitrile of the acetyl derivative of ricinoleic acid (V).

An attempt to prepare phenyl ricinoleate by the action of phenol and phosphorus pentachloride on the acid in a xylene medium gave only octadeca-9,11-dienoic acid.

Tests of the compounds obtained for chemotherapeutic activity, which were carried out by co-workers of the Chemotherapy Department of our Institute under the direction of G. N. Pershin, showed that the majority

of them had a weak activity against tuberculosis bacilli and pathogenic fungi. Ricinoleic acid was found to be most active against tuberculosis (in a dilution of 1 : 409,600), but this activity fell in the presence of serum (dilution 1 : 10,000). Ricinoleic acid also has a weak activity against influenza virus.

EXPERIMENTAL

Amide of ricinoleic acid (I). Methyl ricinoleate (25.3 g) was shaken with 50 ml of methanol (saturated with ammonia) at room temperature for 48 hours. After evaporation of the reaction mass in vacuum, the residue (a waxy mass) was collected and recrystallized from ligroin. We obtained 6 g of (I) with m. p. 64 to 65.5° (according to literature data [9]: m. p. 63.5°).

Preparation of ricinoleic ester of ricinoleic amide (IV). The amide of ricinoleic acid (6 g) was vacuum distilled (200 mm residual pressure). The oily liquid obtained was fractionated. We obtained 3.2 g of (IV) with b. p. 215-220° at 20 mm.

Found %: C 74.85; H 11.64; N 2.64. $C_{36}H_{67}O_4N$. Calculated %: C 74.87; H 11.61; N 2.43.

Nitrile of 12-acetylricinoleic acid (V). A mixture of 21 g of the amide of ricinoleic acid and 15 g of acetic anhydride was heated at 160° for 1 hour. The reaction mixture was evaporated in vacuum and the residue distilled. We obtained 13.9 g of (V) with b. p. 166-170° at 0.8 mm.

Found %: C 75.24; H 11.25; N 3.71. $C_{20}H_{35}O_2N$. Calculated %: C 74.70; H 10.98; N 4.36.

Hydrazide of ricinoleic acid (II). To a solution of 2.4 g of hydrazine hydrate in 20 ml of anhydrous methanol was slowly added 10 g of methyl ricinoleate with stirring. The mixture was boiled for 1.5 hours. After the reaction mixture had been evaporated in vacuum, the residual waxy substance was recrystallized from anhydrous alcohol. We obtained 4.87 g of (II). It formed colorless prisms with m. p. 99-100°, which were readily soluble in acetone and acetic acid and in most normal organic solvents on heating; they were insoluble in water.

Found %: C 69.90, 69.97; H 10.90, 11.69. $C_{18}H_{36}O_2N_2$. Calculated %: C 69.17; H 11.30.

Phenyl ester of octadeca-9,11-dienoic acid (III). To a solution of 16 g of ricinoleic acid in 40 ml of anhydrous benzene at room temperature was slowly added 25.6 g of thionyl chloride with stirring. Stirring was continued for 4 hours. The residue after removal of the benzene was vacuum distilled. The fraction boiling over the range 170-200° at 0.4 mm (4.76 g) was slowly added with stirring to a solution of 6.1 g of phenol in 50 ml of anhydrous toluene. The reaction mixture was boiled for 18 hours. The toluene was removed in vacuum and the residue vacuum distilled. We obtained 4.65 g of (III) with b. p. 223-224° at 0.75 mm.

Found %: C 80.59; H 10.21. $C_{24}H_{36}O_2$. Calculated %: C 80.90; H 10.11.

SUMMARY

1. We prepared the hydrazide of ricinoleic acid, the nitrile of 12-acetylricinoleic acid, the ricinoleic ester of ricinoleic amide, and the phenyl ester of octadeca-9,11-dienoic acid, which have not been described in the literature.

2. It was shown that due to the hydroxyl group on C_{12}, ricinoleic acid derivatives readily lose water to form derivatives of octadeca-9,11-dienoic acid.

3. Tests of the compounds obtained for chemotherapeutic activity showed that some of them have a weak antituberculosis and antifungal action.

LITERATURE CITED

1. W. P. Larson and E. Nelson, Proc. Soc. Exp. Biol. Med. 22, 357 (1925); Chem. Zentr. (1926), I, 3244; W. P. Larson, R. D. Evans, and E. Nelson, Proc. Soc. Exp. Biol. Med. 22, 194 (1926); Chem. Zentr. (1926), II, 442.

2. H. J. Fournell and H. Macy, Am. J. Pub. Health 40, 934; Chem. Abs. 44, 9508d (1950).
3. Y. Miyahara, Ann. Phytopathol. Soc. Japan 18, 37 (1954); Chem. Abs. 48, 8872i (1954).
4. H. Violle, Compt. rend. soc. biol. 123, 448 (1936); Chem. Abs. 31, 757 (1937).
5. C. C. Stock, and T. Francis, J. Exptl. Med. 77, 323 (1943); Chem. Abs. 37, 3168 (1943).
6. V. I. Tovarnitskii, Zhur. Mikrobiol. Épidem. Immunobiol. 11, 93 (1950).
7. K. Burschkies and C. Scholten, Naturw. 31, 591 (1934); Chem. Abs. 38, 5001 (1944).
8. E. Hesse and G. Meissner, Deut. med. Wochschr. 66, 407 (1940); Chem. Abs. 34, 8061 (1940).
9. Ann. Office nat. Combustibles Liquides 9, 663 (1934); Chem. Zentr. (1935), I, 1532.

SYNTHESIS OF ANALOGS OF SOME NATURAL COMPOUNDS

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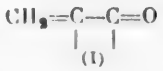
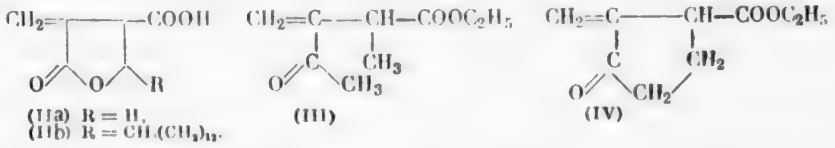
A whole series of natural compounds with biological activity have been found to contain an α-methylene-carbonyl group (I) [1].



(I)

These include protolichesterinic acid [2] and sarcomycin [3]. Compounds close to them in structure and retaining this grouping (I) are of some interest. In this connection, we undertook the synthesis of previously undescribed α-methylene-β-carboxy-γ-butyrolactone (IIa), the first representative in the series of natural lactones of the protolichesterinic acid type (IIb) [4], and the ethyl ester of α-methyl-β-methylenelevulinic acid (III), which may be regarded as the open analog of the ethyl ester of sarcomycin (IV) [5].

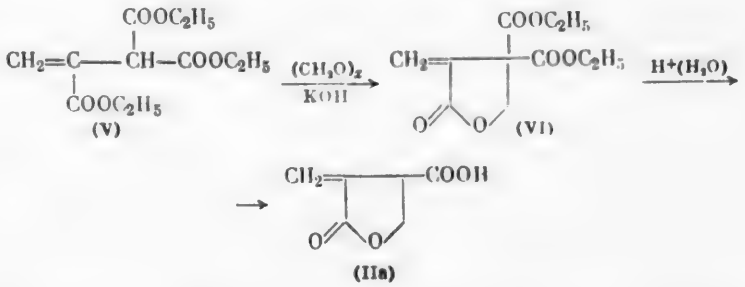


(IIa) R = H,
(IIb) R = $CH_3(CH_2)_{12}$.

(III)

(IV)

α-Methylene-β-carboxy-γ-butyrolactone (IIa) was synthesized in the following way. 2,3,3-tricarbethoxypropene-1 (V) [6] was condensed with paraformaldehyde in the presence of catalytic amounts of alkali to form lactone (VI), which was hydrolyzed and decarboxylated to lactone (IIa) by heating with 20% HCl.



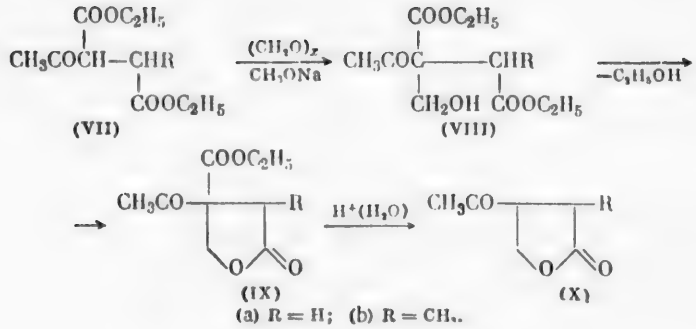
(V)

(VI)

(IIa)

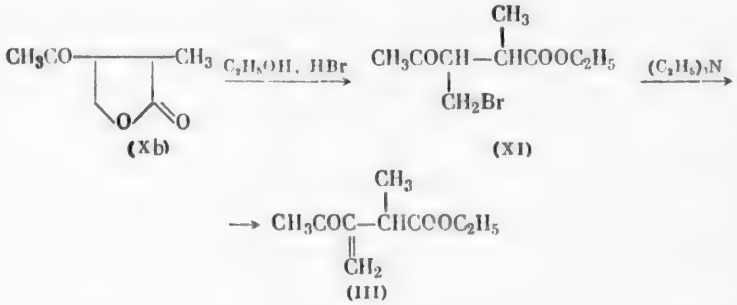
The presence of a semicyclic double bond in the compound obtained (IIa) was confirmed by ozonolysis, from which formaldehyde was isolated as the dimedon derivative.

The method of preparing α-methylene-β-carboxy-γ-butyrolactone (IIa) was extended to the synthesis of β-acetyl-γ-butyrolactones (X).



The diethyl ester of acetylsuccinic acid (VII) was condensed with paraformaldehyde in the presence of catalytic amounts of sodium methylate to form lactones (IX) as a result of the elimination of a molecule of alcohol from hydroxy esters (VIII), formed as intermediates. When heated with 25% HCl at 50-60°, lactones (IX) were converted into β-acetyl-γ-butyrolactones (X). The method developed is simple, gives high yields of β-acetyl-γ-butyrolactones (X), and can probably be used for the synthesis of other compounds of a similar type.

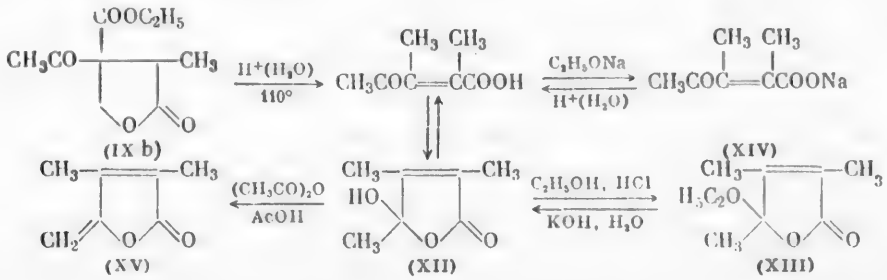
When α-methyl-β-acetyl-γ-butyrolactone (Xb) was kept in 50% alcohol solution of HBr, the lactone ring was opened with the formation of the ethyl ester of α-methyl-β-bromomethyllevulinic acid (XI) and treatment of this with triethylamine gave the ethyl ester of α-methyl-β-methylenelevulinic acid (III).



Ester (III) gave a hydroxamic acid reaction, formed normal derivatives at the carbonyl group, decolorized a solution of bromine in CCl_4, and had an ultraviolet absorption maximum at 216 mμ. When ester (III) was ozonolyzed, we isolated formaldehyde as the dimedon derivative and this confirmed the presence of the methylene double bond.

It is interesting to note that hydrolysis of lactone (IXb) under more drastic conditions (boiling with 20% HCl) yielded not β-acetyl-γ-butyrolactone (Xb), but α,β-dimethylacetylacrylic acid (XII), which exists in the hydroxy lactone form characteristic of acetylacrylic acids [7].

Treatment of acid (XII) with an alcohol solution of HCl yielded its ethyl ester (XIII), which, like the acid itself, did not give a semicarbazone or 2,4-dinitrophenylhydrazone and this may be regarded as a definite demonstration of its hydroxy lactone structure.



Hydrolysis of ester (XIII) with an aqueous solution of alkali and acidification yielded the starting lactone (XII). It is probable that the action of an alcohol solution of sodium ethylate on hydroxy lactone (XII) opened the lactone ring and formed the sodium salt of the acetylacrylic acid (XIV), which was converted to the starting compound (XII) on acidification. Dehydration of hydroxy lactone (XII) by heating in a mixture of acetic anhydride and acetic acid yielded α, β-dimethyl- γ-methylene- $\Delta^{\alpha,\beta}$- γ-butyrolactone (XV), a close analog of protoanemonin [7].

Lactone (XV) was extremely readily polymerized, rapidly decolorized a solution of bromine in CCl_4, and had an ultraviolet absorption maximum at about 260 mμ, which is characteristic of compounds of this type [8].

EXPERIMENTAL

α-Methylene-β,β-dicarbethoxy- γ-butyrolactone (VI). Over a period of 10 minutes, a solution of 0.8 g of KOH in 1 ml of water was added with stirring to a mixture of 91 g of 2,3,3-tricarbethoxypropene-1 (V), 13 g of paraformaldehyde, 130 ml of ethyl acetate, and 30 ml of anhydrous alcohol, heated to 60°. The reaction mixture was then kept at 60° for 5 minutes, 4 ml of concentrated HCl added, and the mixture cooled, filtered, and evaporated in vacuum at 40-70°. Fractionation yielded 60 g (72%) of lactone with b. p. 107-110° (0.5 mm), $n^{20}D$ 1.4590.

α-Methylene-β-carboxy- γ-butyrolactone (IIa). A mixture of 21 g of lactone (VI) and 400 ml of 20% HCl was stirred at 40° for 48 hours. The reaction mixture was decolorized with charcoal, filtered, and evaporated in vacuum at 35°. The residue crystallized when triturated with ether. We obtained 6 g (49%) of acid (IIa) with m. p. 109° (from ether).

Found %: C 50.63; H 4.17. M 142 (titration). $C_6H_6O_4$. Calculated %: C 50.70; H 4.23. M 142.

Ozonolysis of lactono acid (IIa). A solution of 0.3 g of lactono acid (IIa) in 15 ml of ethyl acetate was ozonized for 6 minutes at a rate of 1 mmole per 3 minutes at room temperature. The solution was then poured into 15 ml of water containing 500 mg of zinc dust and boiled for 30 minutes. The hot solution was filtered into a solution of 450 mg of dimedon in 15 ml of alcohol. Crystallization began immediately when 30 ml of water was added. The precipitate was collected and washed with alcohol and ether. We obtained 0.28 g of the dimedon derivative of formaldehyde. It had m. p. 190° (from alcohol).

β-Acetyl-β-carbethoxy- γ-butyrolactone (IXa). To a mixture of 273 g of diethyl α-carbethoxysuccinate (VIIa) and 39 g of paraformaldehyde was gradually added a solution of 0.3 g of sodium in 15 ml of methanol. The mixture was then heated at 50° for 8 hours, cooled, diluted with ether, acidified with 6 N H_2SO_4, filtered, washed with water, and dried with Na_2SO_4. The ether was removed in vacuum and the residue distilled to yield 204 g (80%) of lactone (IXa) with b. p. 123-125° (1 mm), $n^{22}D$ 1.4580.

α-Methyl-β-acetyl-β-carbethoxy-γ-butyrolactone (IXb) was obtained analogously from the diethyl ester of α-methyl-α'-carbethoxysuccinic acid in 75% yield; it had b. p. 123-127° (2 mm), $n^{20}D$ 1.4585.

β-Acetyl- γ-butyrolactone (Xa). A mixture of 202 g of lactone (IXa) and 2.1 liters of 25% HCl was stirred at 55° for 55 hours, decolorized with charcoal, filtered, and evaporated in vacuum at 40-50°. Distillation yielded 97.5 g (76%) of lactone (Xa) with b. p. 114-116° (1 mm), $n^{20}D$ 1.4680.

The semicarbazone of lactone (Xa) melted at 178° (decomp.) (from aqueous alcohol).

Found %: C 45.38; H 6.10; N 22.8. $C_7H_{11}O_3N_3$. Calculated %: C 45.42; H 5.95; N 22.7.

The 2,4-dinitrophenylhydrazone melted at 190° (alcohol – acetic acid) [9].

α-Methyl-β-acetyl- γ-butyrolactone (Xb) was obtained analogously from lactone (IXb) in 77% yield; it had b. p. 108-112° (1 mm), $n^{22}D$ 1.4585.

Found: M 142 (back titration). $C_7H_{10}O_3$. Calculated: M 142.

The semicarbazone of lactone (Xb) melted at 190° (decomp.) (from 75% aqueous alcohol).

Found %: C 48.57; H 6.74; N 21.16. $C_8H_{13}O_3N_3$. Calculated %: C 48.24; H 6.55; N 21.10.

Ethyl ester of α-methyl-β-bromomethyllevulinic acid (XI). A mixture of 11 g of lactone (Xb) and 45 ml of 50% alcohol solution of HBr was kept at 0° for 5 days and then poured into water with ice (55 g) and extracted 4 times with 50 ml portions of ether. The ether extracts were combined, washed twice with 15 ml portions of water, and dried with Na_2SO_4. The ether was evaporated in vacuum at room temperature to yield 12.4 g of the ester of the bromo acid (XI) as a light yellow oil, which readily decomposed during storage with the evolution of hydrogen bromide; it had $n^{20}D$ 1.4800.

Ethyl ester of α-methyl-β-methylenelevulinic acid (III). A mixture of 9.6 g of the ethyl ester of the bromo acid (XI), 10 ml of ether, and 8 g of triethylamine was left at room temperature overnight and then stirred at 35° for 4 hours, cooled, diluted with 100 ml of ether, filtered, washed successively with 8% HCl and water, and dried with Na_2SO_4. The ether solution was evaporated in vacuum at 34° and distillation yielded 3 g (46%) of ester (III) as a clear, mobile oil, which was stable during storage.

B. p. 52-53° (0.5 mm), $n^{20}D$ 1.4450, d^{20}_4 1.011, MR_D 44.7; calc. 44.9. λ_{max} 216 mμ.

Found: M 168 (cryoscopically). $C_9H_{14}O_3$. Calculated: M 170.

The 2,4-dinitrophenylhydrazone of ester (III) melted at 110° (from 75% aqueous alcohol). λ_{max} 268 mμ; log ε 4.4 (alcohol).

Found %: C 51.29; H 5.30. N 16.14. $C_{15}H_{18}O_6N_4$. Calculated %: C 51.42; H 5.18; N 16.0.

The semicarbazone melted at 170° (from alcohol).

Found %: N 18.20. $C_{10}H_{17}O_3N_3$. Calculated %: N 18.50.

Ozonolysis of the ethyl ester of α-methyl-β-methylenelevulinic acid (III). Ester (III) (0.3 g) in 15 ml of ethyl acetate was ozonized for 4.5 minutes at a rate of 2 mmole per 3 minutes at room temperature. The solution became lemon yellow. When the ozone had been passed, 15 ml of water and 500 mg of zinc dust were added to the ethyl acetate solution. The mixture was boiled for 25 minutes. The hot solution was filtered into a solution of 450 mg of dimedon in 15 ml of alcohol and 30 ml of water added.

We obtained 80 mg of the dimedon derivative of formaldehyde with m. p. 189° (from 75% alcohol).

α, β-Dimethylacetylacrylic acid (XII). A mixture of 52 g of lactone (IXb) and 375 ml of 20% HCl was boiled for 35 hours. The solution obtained was decolorized with charcoal, filtered, and evaporated in vacuum. Distillation yielded 30 g (87%) of acid (XII) with b. p. 127-130° (3 mm) and m. p. 65° (from ether).

Found %: C 58.85; H 7.10. $C_7H_{10}O_3$. Calculated %: C 59.10; H 7.05.

Ethyl ester of α, β-dimethylacetylacrylic acid (XIII). A mixture of 6.4 g of α,β-dimethylacetylacrylic acid (XII) and 65 ml of 20% alcohol solution of HCl was left at room temperature for 5 days. The mixture was evaporated in vacuum. Distillation yielded 7 g (91%) of ester (XIII) with b. p. 83° (4 mm), $n^{20}D$ 1.4530.

Found %: C 63.24; H 8.15. M 172 (cryoscopically in benzene). $C_9H_{14}O_3$. Calculated %: C 63.52; H 8.25. M 170.

Sodium salt of α, β-dimethylacetylacrylic acid (XIV). A solution of sodium ethylate (2.0 g of sodium in 45 ml of alcohol) was gradually added with shaking to 13 g of α,β-dimethylacetylacrylic acid (XII) in 12 ml of anhydrous alcohol at 5°. The precipitated salt was collected, washed with alcohol and ether, and dried over P_2O_5 in vacuum. We obtained 11 g (73.5%) of the sodium salt (XIV), which was not hygroscopic, dissolved very readily in water, and gave the starting acid on acidification.

Found %: Na 13.75. M 163 (by titration with 0.1 N HCl to bromophenol blue). $C_7H_9O_3$. Calculated %: Na 14.01. M 164.

Hydrolysis of ethyl ester of α, β-dimethylacetylacrylic acid. A mixture of 5.3 g of ester (XIII), 10 ml of 4 N NaOH, and 4 ml of water was shaken for 1 hour at 70° and left at room temperature overnight. The homogeneous solution was then washed with ether, saturated with ammonium sulfate, and acidified with hydrochloric acid. The reaction mixture was extracted three times with ether (30 ml portions) and the combined ether extracts were washed with water and dried with Na_2SO_4. The ether solution was evaporated to yield 1.4 g (31.6%) of acid (XII) with m. p. 65° (from ether).

α, β-Dimethyl-γ-methylene-$\Delta^{\alpha,\beta}$-γ-butyrolactone (XV). To a mixture of 5 g of α, β-dimethylacetylacrylic acid (XII), 10 ml of acetic anhydride, and 20 ml of glacial acetic acid was added 7 drops of concentrated H_2SO_4. There was strong evolution of heat. The mixture was heated for 1 hour at 90° and then poured into 350 ml of water with ice, neutralized with $NaHCO_3$, and extracted with ether (2 × 100 ml). The ether extracts were combined, washed with water, and dried with Na_2SO_4. The ether solution was evaporated in vacuum at room temperature; the residual red oil was distilled to yield 3.5 g (80%) of lactone (XV) with b. p. 45-47° (2 mm). Lactone (XV) was soluble in the normal organic solvents, rapidly decolorized a solution of bromine in CCl_4, and polymerized very readily. λ_{max} 262 mμ; log ε 4.17.

Found %: C 67.02; H 6.60. $C_7H_8O_2$. Calculated %: C 67.70; H 6.50.

SUMMARY

1. We synthesized the following analogs of some natural compounds which have not been described previously: α-methylene-β-carboxy-γ-butyrolactone, the ethyl ester of α-methyl-β-methylenelevulinic acid, and α,β-dimethyl-γ-methylene-$\Delta^{\alpha,\beta}$-γ-butyrolactone.

2. A method of preparing β-acetyl-γ-butyrolactones was developed.

LITERATURE CITED

1. P. C. Wailes, M. C. Whiting, and L. Fowden, Nature 174, 130 (1954); L. Ruzicka and P. Pieth, Helv. Chim. Acta 14, 1090 (1931); G. Büchi and D. Rosenthal, J. Am. Chem. Soc. 78, 3860 (1956); C. J. Cavallito, D. M. Fruehauf, and I. H. Bailey, J. Am. Chem. Soc. 70, 3724 (1948).
2. Y. Asahina and M. Asano, J. Pharm. Soc. Japan 539, 1 (1927).
3. J. R. Hooper, L. C. Cheney, M. I. Cron, O. B. Fardig, D. A. Johnson, F. M. Palermiti, H. Schmitz, and W. B. Wheatley, Antib. and Chemother. 5, 585 (1955).
4. Y. Asahina, M. Yanagita, and Y. Sacura, Ber. 70, 227 (1937); E. E. van Tamelen and B. S. Rosenberg, J. Am. Chem. Soc. 80, 3079 (1958).
5. Katsuyki Toki, Bull. Chem. Soc. Japan 30, 450 (1957).
6. R. Malachowski and W. Czornodola, Ber. 68, 363 (1935).
7. Shaw, J. Am. Chem. Soc. 68, 2510 (1946).
8. E. Stöcklmayer and T. Meinhard, Scientia pharmac. 23, 212 (1955) Wien; E. Buchta and J. Satzinger, Ber. 2, 471 (1959).
9. B. R. Baker, R. E. Schaul, and I. H. Williams, J. Org. Chem. 17, 126 (1952).

LETTERS TO THE EDITOR

ELECTRONEGATIVITY OF ELEMENTS AND THE FORMATION OF INORGANIC RINGS AND CHAINS

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In the Periodic Table, the electronegativity of the elements ($\underline{x}$) on Pauling's scale [1, 2] varies from $x = 0.75$ for Cs to $x = 4.0$ for F. Lower values of $\underline{x}$ correspond to the tendency of the element to donate electrons, and higher values, to the tendency of the element to accept electrons. The arithmetic mean of x_{Cs} and x_F is 2.4. The electronegativity of carbon equals 2.5, i.e., carbon has the least tendency to accept or donate electrons. This explains the remarkable capacity of carbon to form chains and rings. Consequently, rings or chains formed from atoms of an element with $x > 2.5$ (electronegative metalloids, e.g., O and N) are not stable due to the tendency to accept electrons. On the other hand, rings and chains consisting of atoms of an element with $x < 2.5$ ("electropositive" metalloids, e.g., B, Si, P, Ge, As, and Sb) are not stable due to the tendency to donate electrons. Obviously, with an alternation of elements A and B with $x_A < 2.5$ and $x_B > 2.5$ it may be possible to achieve compensation, which leads to stabilization of the ring or chain. In actual fact, the literature contains descriptions of inorganic rings [3] and chains [4] formed by alternation of such elements. The table gives the electronegativities of a number of pairs of elements calculated by the formula:

$$x_{AB} = \frac{x_A + x_B}{2}.$$

Element B	Element A x								
	B 2.0	C 2.5	Si 1.8	P 2.1	S 2.5	Ge 1.8	As 2.0	Se 2.4	Sb 2.1
O x = 3.5	2.75	3.0	2.6	2.8	3.0	2.6	2.75	2.85	2.8
N x = 3.0	2.5	2.75	2.4	2.6	2.75	2.4	2.5	2.7	2.55
S x = 2.5	2.25	2.5	2.15	2.3	2.5	2.15	2.25	2.45	2.3

The heavy figures denote values of $\bar{x}_{AB}$ for which inorganic rings or chains formed by alternation are known.

It may be stated that those elements which satisfy the equation $\bar{x}_{AB} = 2.5 \pm 0.35$ (where $2.5 = x_C$) may form inorganic rings or chains. This becomes more obvious if we calculate the value of $\bar{x}_{AB}$ for pairs of elements which do not form rings or chains, where $\bar{x}_{AB} > 2.85$ or $\bar{x}_{AB} < 2.15$ (e.g., for Si–P, $\bar{x} = 1.95$).

The rule reported makes it possible to predict which elements may form inorganic rings or chains. Thus, it may be expected that new inorganic cyclic or high-molecular compounds may be obtained with Ge–N, Ge–S, As–N, Sb–N, etc., units, which have not been described in the literature up to now.

LITERATURE CITED

1. L. Pauling, The Nature of the Chemical Bond [Russian translation] (Moscow, 1950).
2. W. Gordy and W. J. O. Thomas, J. Chem. Phys. 24, 439 (1956).
3. I. Haiduc, Rev. Chim. Bucharest 7, 721 (1956).
4. Diploma work, Monograph "Inorganic Cyclic Compounds" (300 pages) (Kept in the Chemistry Faculty Library of Cluj University); V. V. Korshak and K. K. Mozgova, Usp. Khim. 28, 783 (1959).

COMPETITIONS FOR NAMED PRIZES OF THE ACADEMY OF SCIENCES, USSR

The Division of Chemical Sciences of the Acad. Sci. USSR advises that: 1) in connection with the centennial of the birth of Academician N. S. Kurnakov, a competition will be held on December 6, 1960 for the Academy of Sciences N. S. Kurnakov Prize of 10,000 rubles to be won by a Soviet scientist for outstanding work in the field of general chemistry, physicochemical analysis and its application; 2) a competition will be held on February 6, 1961 for the Academy of Sciences N. D. Zelinskii Prize of 10,000 rubles to be won by a Soviet scientist for outstanding work in the field of organic chemistry and petroleum chemistry.

Material for the competition must be submitted to the Division of Chemical Sciences, Academy of Sciences, USSR not later than three months prior to the date of the award of the corresponding prize.

The address of the Division of Chemical Sciences is:

Moscow, B-71, Lenin Prospect, 14.

Organizations and individuals proposing candidates for a particular prize must forward to the Division of Chemical Sciences the following documents and materials, marked "for the competition for the .... prize:"

a) published scientific work and material on scientific discoveries or inventions in three copies in any language;

b) arguments on the scientific value of the work submitted;

c) author's abstract of scientific work up to a quarter of its length;

d) brief biographical information on the candidate, listing his main scientific work, discoveries, and inventions.

Footnote: work for which a prize has already been awarded will not be accepted for the competition.

Division of Chemical Sciences
Academy of Sciences, USSR

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.